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THE HISTORIC EVOLUTION OF VARIOLATION.*†

By Arnold C. Klebs, M. D., Lausanne, Switzerland.

Immunology, the latest child of medical science, has reached, after a short existence, a very considerable development, some even think maturity. However true this may be, its creation has certainly called forth efforts of the most varied nature embracing and mobilizing almost all branches of physical sciences. The very acuteness of these efforts is inimical to retrospection. Only very recently some experimenters have searched the earlier literature, of vaccination for instance,[1] for support of their conception. Variolation has entered very little, if at all, into such investigations and it is really astonishing how thoroughly it is forgotten, this most interesting epoch in medical history, which kept greater and humbler minds in fever heat during almost one whole century. This oblivion is particularly curious because variolation called forth a unique and extensive trial of a specific preventive method, the logical consequence of which was vaccination. This fact does not detract from the merits of Jenner, who by observation and conclusive experiment was enabled to render an immortal service. It is true that Jenner was unaware of the generic identity of vaccinia and variola, that to him cowpox was a disease *sui generis*, the inoculation of which conferred immunity to smallpox for some unknown mysterious reason. It is this conception which stamped vaccination as a new departure and it is largely responsible for the oblivion into which variolation has fallen. Jenner's belief[2] in the common derivation of cowpox and smallpox from the grease of horses, and Pearson's and Baron's vague suspicions of a more intimate relationship between variola and vaccinia, passed unnoticed for almost another century, after which the intrinsic analogy of variolation and vaccination could be demonstrated.

In searching for the earliest origins of variolation I may cite the words of Sir George Baker,[3] one of the most scientific inoculators of his time: "It cannot but be acknowledged that the art of Medicine has, in several instances, been greatly indebted to accident and that some of its most valuable improvements have been received from the hands of Ignorance and Barbarism." This indebtedness to the intuitive genius of popular reason and procedure is strikingly illustrated in the reports of early practice of variolation. While the learned since oldest times strained every effort towards the discovery of a Medicinal antidote, the simple-minded evolved the idea of protective inoculation. It is difficult to ascertain any one locality where variolation was first practised. From its wide distribution it would seem that it arose spontaneously in various places where the need for it occurred. The earliest alleged reference to variolation in the chronicles of the 6th century by Marius, Bishop of Avenches, I have been unable to verify.[4] I found only the well known report of a deadly

* Authors in 18th century literature speak only of "inoculation" (ingrafting, insertion). At present for the sake of clearness the term "variolation" seems preferable. In retrospective reviews of the subject the term vaccination is often used erroneously for variolation and a similar confusion is likely to occur if modern writers persist in using faultily the words "vaccine and vaccination" for protective and therapeutic inoculation generally.

† Paper read before The Johns Hopkins Hospital Historical Club, October 14, 1912.

[1] von Pirquet, *op. cit.*, introduction.

[2] Jenner, Inquiry, 1798, 3d paragraph.

[3] G. Baker, An inquiry, etc., 1766, p. 1.

[4] Edit. Bouquet, Histoire des Gaules, II, 12.

epidemic (570 and 571 A. D.) in Italy and Gaul of a disease which for the first time is called "variola."[5] Clearly referring to variolation is a remarkable verse of the School of Salerno[6] (10th or 11th century) entitled *adversus variola* and which runs as follows:

Ne pariant teneris variolae funera natis
Illorum venis variolas mitte salubres.
Seu potius morbi contagia tangere vitent
Aegrum aegrique halitus, velamina, lintea, vestes
Ipseque quae tetigit male pura corpora dextra.[7]

For preventive purposes the voluntary transference of a benign variola is surely recommended here, the *venis*, however, may indicate "system" generally, in which case the disease is to be transmitted by simple exposure or we may take it more literally and an operation then suggests itself. The last three lines giving preference in very modern-sounding language to the avoidance of infection by contact, seems to me to lend strength to the latter interpretation.

The first authentic reports of this practice we find in the Ephemerides of the Academia Cæsarea Leopoldino-Carolina published at Leipzig between 1670 and 1705. Here Dr. Vollgnad of Breslau[8] in 1671 and Dr. Schultz of Thorn in 1677 clearly report instances of the custom of "buying the smallpox." There is, however, no reference made to the actual inoculation with the pock scabs purchased in the plague house, but that such was done is very likely, since Schultz speaks of the rather serious illness which his own brother acquired in this manner. It does not seem to me that these cases have anything to do with the sympathetic transference of disease, which agitated some medical minds of the day, and as instances of which they obviously were reported. Creighton[9] gives an interesting example of this form of transplantation in 1657: "Some persons in the smallpox keep a sheep or a wether beside them in the chamber, those animals being apt to receive the envenomed matter and draw it to themselves"—only a slight modification of the Jewish scape-goat! Of course this has as little to do with variolation as the Biblical passage cited by Massey in 1722 in condemnation of inoculation: "So went Satan forth from the presence of the Lord and smote Job with sore boils from the soles of his feet unto his crown" (Job, II, 7).

[5] Smallpox is hereby not defined with any certainty. Its root *varus* as used by Celsus and Pliny is meant to indicate a pustulous disease, especially of the face.

[6] S. de Renzi, Flos Medicinae Scholae Salerni, Naples 1859, p. 90 (3059, *et seq.*). A footnote of the editor gives as his opinion that the first two lines refer to variolation, which was not invented in the 18th century, or in Greece, but is older.

[7] This may be rendered: In order that variola may not produce death among tender babes, put into their veins a favorable variola. Better still they should avoid touching the contagium of the disease: the sick person, the breath of the sick, the clothes, the coverings, the garments and such clean bodies as he may have infected (*tetigit male*) with his hand.

[8] H. Vollgnad (1634-1682), member of Academy, 1669.

[9] Slatholm (Buntingford), 1657, cited in Creighton, History of Epidemics in Britain, p. 475.

Further reports of the ancient practice all date from the time of the medical introduction of variolation to Europe and America. They were of the usual order, meant to show that there is nothing new under the sun and some of them, therefore, have to be taken with caution. Thus we hear of a crude variolation in Scotland (Monro I., & Kennedy), in Wales (Perrot Williams),[10] in Auvergne and Perigord (de la Condamine), in Jutland (Bartholin), in the Duchy of Cleve (Schwencke) and other parts of Germany. Of the inoculations practised in Greece, whence it was introduced to Western Europe by way of Constantinople, I shall speak later. The earliest traces of variolation are found in Asia and in Africa. In Africa the practice continues to this day among certain tribes, chiefly negroes, in the eastern, central and western regions. On the White Nile in the equatorial province (Welson & Felkin) among the Bari, and further east among the Somali (Stahlmann) a similar custom is found. It seems to have been highly developed by the most important of the native Bantu tribes, the Baganda, living northwest of Lake Victoria in the old Kingdom of Uganda. Further west we find the Wanjamwesi, and in the Sudan the Ashanti, and some Moorish tribes practice inoculation on their children. From northern Africa we have the report of the Tripolitan Ambassador, Kassem Aga, which made the round of 18th century literature, about the ancient variolation by Mohammedan tribes in Tripolis, Tunis and the Kabyl mountains. Not long ago we had a verification of this latter report by a French naval physician, Dr. H. Gros,[11] stationed at Rébéval in Algeria. He has observed a considerable number of variolations practised by Arabs and Kabyles and curiously enough comes to the conclusion that variolation ought to be resorted to if, for some reason or other, the supply of vaccine became exhausted. This account contains many interesting observations which corroborate most of the historical records of the 18th century.[12]

Exceedingly interesting accounts about smallpox inoculations are available from Asia. I can only briefly refer to them. China, of course, again is said to have known variolation since remotest times. We have no reliable data as to the age and extent of the practice; we must be satisfied with the knowledge that a method of inoculating the virus into the skin or in the form of dry powder blown into the nostrils, has been known to exist before it reached Europe.[13] In India a similar method seems to have been carried out on a systematic plan by special delegates of the Brahmin caste in conjunction with a religious cult of the smallpox deity.[14]

[10] Philos. Transact., 1722.

[11] La variolisation, Janus, 1902, VII, 169.

[12] Other reports from travellers about variolation: Bruce (1790), Levaillant (1790-1796), Michaux (ab. 1800) for Africa, Cook (ab. 1780) for Senegambia, Barbary, Bengal.

[13] The "Tchan-teoo" or "sowing the smallpox" in d'Entrecolles, Lettres édif. et cur. des missions 1726, XX, 34 (from Pekin) and other reports in same letters.

[14] Holwell, *op. cit.* Also J. Moore, History of the Smallpox, Lond., 1815, 26-34, with plate representing the religious rite, from a Hindu drawing in the library of Mrs. Bliss of Kensington.

None of these primitive variolations served to acquaint Western Europe with the practice. Only after it had reached a certain development in Constantinople could it be studied, reported and recommended. From this city Lady Mary Wortley Montagu, wife of the British Ambassador to the Porte, wrote to her friends at home about the method of inoculation as practised under her eyes and expressed her intention (to Sarah Chiswell, April 1, 1717, from Adrianople) of introducing it to England. She even caused the inoculation of her three-year old son Edward, by a Greek woman with Maitland's assistance,[15] and influenced that of the three children of the Marquis de Châteauneuf, Secretary to the French Embassy at about the same time (1718). Her inspiration and these examples undoubtedly opened the doors for the introduction of the practice in England. There was already some medical agitation on the subject, before Lady Mary became interested, and it can safely be presumed that she was not ignorant of it. Dr. Timoni, a Greek physician of Constantinople educated at Oxford, published in 1713 an account of the method of variolation as observed and practised by him. In December of the same year he sent a personal communication on the subject to Dr. Woodward,[16] who read it before the Royal Society. A little earlier a similar report reached the Swedes, sent to them from Bender in Bessarabia by their exiled king, Charles XII, with the recommendation to introduce the method.[17]

Other medical men in England at this time had some personal knowledge of the method which they had seen practised in Constantinople. We know of two, a Dr. Terry of Enfield, who later is consulted about it by Sir Hans Sloane, and a Scotch surgeon, Peter Kennedy,[18] who describes the method in his book in 1715. A dissertation on inoculation appears in Venice by a Dr. Pylarini[19] the next year. A friend and former consular colleague of the latter in Smyrna, Dr. Wm. Sherard, informs Sir Hans Sloane and, through him, the Royal Society, of this publication with details about the method and an account of Dr. Pylarini's experiences. Now the Royal Society becomes really interested and the pages of the Philosophical Transactions of the following years are filled with further accounts, which Douglass of Boston later (1730) characterizes sneeringly as "virtuoso amusements."

At the same time something was heard of the "Greek method" in France. Boyer[20] of Montpellier, later Dean of the Medical Faculty of Paris (1756), had travelled as a young man in the Orient and had there become acquainted with variolation. On his return to Montpellier he studied medicine and wrote his inaugural thesis (1717) on inoculation and the reasons why it might be imitated to great advantage in France. Actual inoculations very probably were practised in Paris at about this time by a Greek physician Carazza. Eller tells us of making his acquaintance there, and how he was taught the method and how he successfully inoculated a child. Although Eller does not mention the exact date, it is evident that it took place in or before 1720, because in that year he went with Lord Peterborough to England and returned from there to Germany in January 1721.[21]

At this moment, when the new method knocked at the doors of the universities, promising fresh hopes but also planting the first seeds of discord among the sister faculties, the 18th century is yet young. The glaring contrasts and contradictions are not as apparent as they will become later, the genius of Newton—he still presides over the Royal Society—is only beginning to assert itself. In medicine Sydenham's influence is paramount, while Boerhaave in Leyden and Morgagni in Padua are training men who are to found modern medical science. Hoffmann and Stahl supply the cravings for theoretical contemplation, while practice continues on old lines. Everywhere reform is in the air, the struggle against superstition and for tolerance has begun. The realization that the riddles of life and its problems are not to be solved by pure metaphysical speculation begins to dawn upon the learned and experiment is more and more resorted to for the final criterion.

From the time of its introduction to the Occident in 1713 to the advent of vaccination in 1798 and its general acceptance in 1840, variolation does not follow a course of steady progress. As we shall see, it enjoys a few years of the success of novelty (until 1727), followed by twenty years (1746) of indifference, after which it slowly gives rise to a remarkable period of serious scientific investigation.

The honors of the first inoculation in the Occident (excepting that by Eller in Paris) will probably best be divided between London and Boston. Dr. Fitz, in an admirable account of the early inoculations in Boston, tends to the belief that Boylston, inspired by Cotton Mather, made his first attempt

[15] Letter to Lord Montagu (of March 23, 1718) at Pera from Belgrad.

[16] John Woodward (1665-1728) excellent geologist, but poor physician. See Creighton's (*op. cit.*, p. 449) amusing account of his duel with Mead in Gresham College where he was professor of physic. Its cause, the smallpox controversy, involved also Friend and later Dover. In 1718 he published a tract "the State of Physick" in which he discussed the "new practice of purgeing" in smallpox.

[17] This report was probably written by the king's physician, Skraggenstyerna.

[18] Peter Kennedy: Essay on external remedies (Chap. 37), 1715.

[19] Pylarini, Nova et tuta, etc., 1715. Sloane in Phil. Trans., XXIX, 1716.

[20] J. B. N. Boyer, 1693-1768.

[21] J. Th. Eller, Observationes cognoscendis et curandis morbis praesertim acutis, Regimont. & Lips, 1762, p. 150. (French transl. Par. 1774.) Eller was born in the Duchy of Anhalt in 1689, became M. D. in 1716 then travelled in Holland and practised in the mines of the Harz Mountains. From here he went to Paris and worked under Hecquet, Astruc, Helvetius and Winslow, giving much attention to surgery, at the Hôtel Dieu and the Salpétrière. In London he frequented Cheselden, Mead, Sloane and Newton. He left London in January, 1721, became court physician in Anhalt, inoculated several persons, and in 1724 he was at the court of Berlin, teaching at the newly founded Medico-Surgical College. He and Stahl (Halle) are largely responsible for the sanitary reform in Prussia, which formed the basis for the present institutions.

without knowing of the inoculations performed in London.[22] There is no direct evidence of his ignorance and he certainly had time to learn about the London inoculations in April and May, since he inoculated his son Thomas and the two slaves on June 26. Undoubtedly he had courage enough to proceed without any other assurance than that of his friends and the older reports at hand, but the situation was precarious and it looks as if the latest news may have been welcome and actually determined him.

The merits of Lady Montagu in inciting the early trials in London were undoubtedly great in that year of 1721, when the smallpox was raging on both sides of the Atlantic. A Portuguese physician in London, à Castro, had anonymously published a pamphlet on the subject in March and Dr. Walter Harris spoke recommendingly of inoculation before the College of Physicians on April 17. Lady Mary probably did not need these learned suggestions to remind her of her experience in the Orient and with the danger of smallpox at the door, she had Maitland inoculate, in April, her four-year old daughter, the future Lady Bute. One of the three interested spectators from the College of Physicians, Dr. Keith, was sufficiently impressed by the harmlessness of the operation to have his own six-year old son inoculated on May 11. In this case, bleeding was resorted to as a preparatory measure and we see herein, as also in similar examples in Boston, the germ of that "preparation" which is to play such an important rôle later on. Lady Mary meanwhile does not stop with the inoculation of her own child; she takes up the personal propaganda begun in her letters from the Orient, she finds it now easy to induce many of her friends to follow her example, but her main efforts she exerts towards winning the court. In this task she is aided by her intimate relationship with the Princess of Wales, later Queen Caroline, whom Voltaire, because of her intelligent interest in arts and sciences, addresses as the "philosopher on the throne." George I is willing to permit the inoculation of his grandchildren but a preliminary experiment is deemed advisable. Here is the first beginning of scientific procedure. Six condemned criminals in Newgate prison are inoculated as test cases, the best medical men of London are watching the experiment, with Mead at their head. Nothing unusual happens; somewhat severe symptoms are observed only in one girl, whom Mead inoculated with dried virus in the nostrils (Chinese method), but she also recovers. One man in whom the inoculation did not "take," is found to have had smallpox before. A further test is made by Mead and Steigerthal, who send one of the inoculated patients to Hertford where a severe epidemic rages; no infection takes place. George I and his court feel reassured by the results of these experiments, and further good reports having reached the town from Halifax, in Yorkshire, where Nettleton had inoculated with satisfactory results since December, the operations on the Princesses Amelia and Caroline take place on April 19, 1722. The surgeon Amyand, attended by Sir Hans Sloane, Teissier and Maitland, performs the inoculation.[23] The immediate result of this evident approval of variolation by the court was that the nobility hastened to follow the august example and so we find the gazettes reporting on these events, mentioning all the names of the ultra-fashionables. The next result was the formation of two opposing factions. Pamphlets were written, sermons preached for and against the new method, mostly by people who knew nothing or next to nothing about inoculation. This condition continues through the whole epoch of variolation and as a matter of fact long after its abandonment. In the vast literature thereby produced it is often exceedingly difficult to find one's way. Wagstaff, the medical satirist, Blackmore, inferior medical author and poet, Clinch, the surgeon, Massey, the apothecary of Christ Hospital, are the chief opponents; the learned Dr. Freind[24] wavers, but objects to the noise made about inoculation, Arbuthnot, friend of Pope and Swift and commentator of Boerhaave, Jurin, secretary of the Royal Society under Newton, Mead and Sloane were, however, more or less active in the recommendation of inoculation.

The arguments brought forth against variolation were, its risks to the individual, the uncertainty of its protective power and the danger of its spreading the disease. The last argument had received support when the news came of an accident that had happened in Maitland's experience at Hertford, where he had gone to inoculate in the autumn of 1721. A child ill with artificial smallpox had infected six servants of whom one had died. This demonstration of the contagiousness of inoculated smallpox offered the strongest point to the cause of the opponents. They, however, resorted oftenest to personal vituperation or bitter condemnation on religious and moral grounds. On the other hand the inoculators and their upholders, although reiterating the most obvious advantages of inoculation, viz., freedom in the selection of appropriate subjects (children), favorable external circumstances (seasons), and careful preparation, resorted almost exclusively to statistical data in their support. Jurin,[25] who excelled in mathematics, soon collected enough cases to figure out the ratios as: One death only in 91 inoculated (two in 182), while the natural smallpox killed one in five or six. He refers to the "letter of Cotton Mather of the 10. March 1721"[26] in which five to six deaths are reported among 300 inoculations, mak-

[22] Professor Kittredge (*op. cit.*) has recently given valuable additional information on the subject of early variolation in Boston. It leads to the conclusion that Cotton Mather's knowledge of it has not been fully recognized and especially that he was acquainted with variolation (among negroes) before he received the reports about it from Europe.

[23] A medal was struck to celebrate the event. *Av.* George I, 1721, *Rev.* Inoculation instituted. (Pfeiffer, 373*a*.)

[24] See reference to John Gaddesden in his "History" (1725): had he "lived in our day, he would, I don't question, have been at the head of the inoculators." (Creighton II, 478.)

[25] Jurin to Cotesworth 1723. James Jurin born 1684, secretary and later president of Royal Society, was one of the first physicians to Guy's Hospital. The advocacy of his "lixivium lithontripticum" brought him questionable fame.

[26] A. L. (contemporary copy) in Sloane MSS. 3324, fol. 260 (see Kittredge, *op. cit.*, p. 477). The letter is also quoted by Douglass in his "dissertation" of 1730.

ing a ratio of one in 60. He concludes from it that inoculators in New England were less careful.[27]

The technique meanwhile had seen considerable deviations from its primitive Greek prototype. In Constantinople, Maitland had already replaced the dirty needle of the woman operator by the lancet. Nettleton, who probably had the largest experience in these early years, thought it important to make rather deep incisions and to keep them open so that the wound would drain freely and allow the morbid humors to escape. The arms or thighs were the favorite regions chosen.[28] The virus was taken directly from a smallpox patient and transferred, or it was collected on threads and dried for later use.

It seems that the inoculations were not often performed by the physicians themselves; they usually had a surgeon do it and watched the case before and after. Thus a type of inoculation specialist was evolved and all sorts of people took it up as a lucrative profession.[29] Some of the failures may easily be attributed to crude methods. Maitland seems to have created the type of the itinerant inoculator, whom we can soon follow all over Europe. We have already encountered Maitland in Hertford; a few years afterwards he is on the continent inoculating Prince Frederick and others at Hanover. After this we find him in Scotland [30] where he has ill-luck, losing one in ten. This experience, the Hertford case, and the deaths of several prominent persons, duly registered in the gazettes, added powerfully to the arguments of the opponents. The subject was brought up in Parliament and inoculation declared dangerous. This was in 1728. Up to that year Jurin [31] could collect in his report 897 known inoculations with 17 deaths, not all directly attributable to the operation. He considered the practice now "exploded," while the otherwise sceptical Douglass [32] admits that the opponents are now prepared to acknowledge that "inoculation, generally speaking, is a more easy way of undergoing smallpox."

The Continent, meanwhile, did hardly more than act the part of the spectator. LeDuc of Constantinople writes the first inaugural thesis on inoculation at Leyden; it is approved on July 28, 1721, and published together with the dissertations of à Castro and Walter Harris of London in 1722. Boerhaave maintained an expectant attitude. We have no reports of his having tried the method himself or persuaded others to do so. Theoretically he surely approved, for we find him saying at the end of his Aphorism 1403 (Edit., Leyd., 1727). *Prophylaxis insitiva videtur satis certa tutaque.* Of his pupils Van Swieten continues in this reserved attitude, while de Haën becomes one of its most persistent opponents and Tronchin one of the most famous inoculators in Europe.

In Germany Eller, whom we have met already in Paris, has returned to his home in Anhalt. As physician to the local court he performs two inoculations, but, soon called to the Prussian court, he is not allowed to see smallpox cases and has to desist. In Breslau reports are received of inoculations performed by one Reimarus in Hungary.[33] In the two universities, Altdorf and Erfurt, which have long ceased to exist, doctor dissertations are published on inoculation by Mülich and Cramer,[34] but they report no new trials. In Hanover, however, the inoculation of Prince Frederick acted as a stimulant. J. E. Wreden publishes a treatise on it and his son John, later body surgeon to the Prince of Wales, soon begins to inoculate.[35] Outside of the Electorate of Hanover, naturally influenced by England, Germany contributes very little to the history of inoculation. Of Austria, Italy and Switzerland I shall speak later. In Sweden we have one publication in 1737 by Spoering, but also no actual inoculation.

The history of variolation in France offers much of interest and forms a valuable contribution to the annals of culture in general. At the time when variolation first appeared in England, medical science and practice in France had made little progress since the days of Ambroise Paré and Guy Patin. Montpellier showed more signs of progressive activity and in later years especially, the children of this Alma Mater were prominent in the ensuing struggle. While in England inoculation occupied minds rather intensely for eight years, only in the one year of 1723 is this subject at all considered in France, particularly in Paris, and then only academically. Louis XV was then thirteen years old and the Duke of Orleans was nearing the end of his regency and his life. Dr. de la Coste, an enthusiast for inoculation, who had followed its introduction to England, writes about it to Dodart,[36] formerly physician to Louis XIV. He tells him all he knows about the subject and especially that the English court is in favor of it. At a solemn meeting at the Sorbonne he explains to the learned dean and nine doctors the evident advantages of inoculation. After a careful analysis of the moral and religious factors involved, it was decided that experiments might be made without interfering seriously with Divine providence. This meeting had the effect of winning over the Regent, who also probably was influenced favorably by Helvetius [37] who was close to him at the time. It therefore looked for a while as if experiments might begin. Then appeared an anonymous pamphlet entitled: *Raisons de doute contre l'inoculation,* in which strong language was used against *la méthode anglaise* and its promoters. It

[27] The figures of Cotton Mather are quoted by the anti-inoculists again and again with considerable success all over Europe.

[28] In the Greek practice the forehead, shoulders, hands and other parts of the body were chosen, the choice being determined on religious grounds and it varied with individual inoculators.

[29] We know of a blacksmith who thus changed his occupation, and a man-servant who gave notice to his employer because he could earn more as an inoculator. (Watts, Watson.)

[30] Alex. Monro I, 1697-1767.

[31] See also Scheuchzer (son of the Zurich naturalist) on success in Great Britain, 1729. Another late endorser of the method was Lobb in 1831. (His treatise on smallpox received the praise of Boerhaave.)

[32] Douglass, 1730, *op. cit.*

[33] Breslauer Versuche, XVII, 253.

[34] 1725 and 1726.

[35] Report in 1739, London.

[36] Cl. J. B. Dodart, 1664-1730.

[37] J. Cl. Adr. Helvetius, 1685-1755.

was soon learned that the author was old Hecquet,[38] dean of the *Faculté de médecine,* more theologian than physician and a stubborn opponent of all innovations. His words carried much weight and when the Regent died on December 3, the chance of inoculation grew very faint and was entirely extinguished at a meeting in the *École de Médecine* on December 30[39] where the *quæstio medica,* worded ominously "Is it a crime to inoculate?" was discussed under the presidency of Claude de la Vigne,[40] the new king's new physician. An interesting contrast: the Sorbonne for, the *École de Médecine* against the new method! As a child Louis XV comes to power; he was of course not to blame in that, for 30 years after his advent, inoculation was hardly mentioned in France, but curiously enough, as a man, after 50 years of a disastrous reign, he falls victim to the very disease the method was intended to prevent. Voltaire, in his apartment quite close to the *École de Médecine,* at this moment is making a very personal and most unpleasant acquaintance with smallpox, nursed by his devoted friend Adrienne Lecouvreur. Two or three years hence he is to begin his eloquent propaganda for inoculation in one of his letters from that England which is to influence so strongly his whole point of view.

During the 20 years following the practical abandonment of inoculation in England, and while next to nothing was done in Europe, events occur in America which later are to help considerably towards a revival of the practice. An epidemic of smallpox in Charleston in 1738 gives the incentive. A surgeon, Mowbray, and a Scotch physician, Kilpatrick (later as Kirkpatrick one of the foremost inoculators in England), inoculate a very considerable number of persons in that year.[41] Mowbray evidently started the inoculations and seems to have done the greatest number. Kilpatrick's account, which was published first in Charleston and then in London in 1743, relates, with great frankness, the successes and failures (about 800 inoculations with eight deaths).[42] They met with distinct opposition, especially on the part of other practitioners.[43] Kilpatrick, in theory, favors careful preparation of the patient before the operation. His guiding principle is the cooling regimen of Sydenham with a "few remedies perhaps" so that the "Solids and Fluids may be reduced from a greater, to less Inflammability." His conception, as these quotations show, is that of his time but he admits, "without prejudice, that preparation was too often neglected with us." We also learn from him, and this is an important innovation, that Mowbray very often inoculated with the virus taken from the pustules of a previous inoculation and that he repeated the process up to six times,[44] without perceiving any reduction of virulence. It would be interesting to enter more fully into the excellent observations of this essay. They are distinctly in advance of the time and I believe mark a more valuable advance in the history of inoculation in America than that presented in a pamphlet of Dr. Adam Thomson, published eight years later and of which Dr. Henry Lee Smith[45] has given a full account. From this "discourse" of Thomson's it appears that he had begun to inoculate in Philadelphia at about the same time when Mowbray and Kilpatrick started their experiments in Charleston. The crux of his method is specific preparation, applying Boerhaave's suggestion that mercury and antimony may act as preventives against smallpox. He lays greater stress on these medicines than does Kilpatrick, otherwise there is no difference between the two methods. There is no doubt that Thomson succeeded in impressing his patients and also some doctors with his method of preparation. Dr. Gale of Connecticut seems to have been his most enthusiastic follower. At least I find him writing to Huxham[46] about it: Boerhaave's "intimation was improved, and mercury introduced into practice, by physicians in the English American Colonies, about 1745. Several American physicians claim the second glory of Boerhaave; perhaps Dr. Thomas (*sic.*) of Virginia, and Dr. Murison of Long Island." Ruston[47] a little later in speaking of this method ascribes it, as does Gale, to Murison and to Dr. Thomson of Virginia. Ruston who is in favor of a mild preparation, shies at this particular one for the secret of which, he says, "considerable premiums were offered." Ten to twenty grains of calomel every other night counteracted by a drastic purgative for two weeks seem to him rather violent as a preparation for more trouble!

We are now nearing the middle of the 18th century. The failures of the introductory period in England were almost forgotten and Europe in general was becoming more and more receptive to such an innovation and, with the increasing restlessness of the age, receptiveness developed into eagerness. In England Kilpatrick's essay (1743) on the experience in South Carolina was very largely responsible for a revival. He had arrived himself and at once set to work as a specialist inoculator. Among those who followed his example are Ranby, Middleton, Hawkins, Frewen, Burges, Archer, etc. The alleged necessity of an elaborate course of preparation on hygienic and medicinal lines, of a surgical operation requiring often a prolonged after-treatment, held out golden promises to physician, surgeon and apothecary. Mercenary calculation therefore entered very largely into the advocacy of "preparation" and deep incisions. It is well to bear this in mind. Some of the more earnest practitioners object to these complications but, in spite of them, this cumbersome procedure maintains its vogue during the following 20 years. The fact that it is very costly rather increases the demand for it among the wealthy and thus it gains influential protectors. This leads to provision for the poor and here the foundation, under the patronage of the Duke of Marlborough,

[38] Phil. Hecquet, 1661-1731.

[39] Duvrac's account, 1755.

[40] Cl. de la Vigne de Frêcheville, 1695-1758.

[41] Kilpatrick, *op. cit.*, p. 44. On May 21, 1738, the first three persons were inoculated in Charleston, the two daughters of a Mrs. Sarah Blakeway and a Miss Baker.

[42] Kilpatrick, *op. cit.*, p. 34.

[43] Kilpatrick, *op. cit.*, p. 44, controversy with Dr. Thomas Dale.

[44] Kilpatrick, *op. cit.*, pp. 49 and 50.

[45] Johns Hopkins Hosp. Bull., 1909, XX, 49.

[46] John Andrew, 1765, *op. cit.*, pp. 9 and 44.

[47] Thomas Ruston, *op. cit.*, p. 2.

of the Middlesex County Hospital for smallpox, and soon afterwards that of others in London,[48] marks an epoch. There was little effort made, at least at first, to utilize these institutions for a scientific study and an improvement of variolation. As each patient, because of the preparation before inoculation, had to stay a very long time, at least while a preparatory period was thought to be necessary, the benefit which the poor derived from these hospitals was very small, because of the few that could be admitted.

The practice of variolation, thus taken up in all earnest by energetic medical men, prevailed in spite of the opposition which continued unabated. The cause found a very valuable champion in Isaac Maddox, Bishop of Worcester, who in his sermons intelligently and forcefully recommended inoculation. Another churchman, de la Faye, on the other hand, used the pulpit for the fiercest denunciation of inoculation and inoculators. In medical circles all the questions involving smallpox and variolation were ventilated. The war of pamphlets is opened by a letter of one Dod Pierce to Pierce Dod, physician of St. Bartholomew and author of "Several cases in physic."[49]

In 1747 Mead's *de variolis* (with the translation of Rhazes' commentary) appears. He devotes a brief chapter (V) to inoculation. He is decidedly in favor of it and does not know of relapses after it. According to him the great advantage of the inoculated disease over the natural one is the opportunity afforded of selecting appropriate subjects and preparing them "by drawing away, where necessary, some blood, and gently purging the humors," in order to "obviate the violence of the approaching fever." He cannot imagine much benefit from the discharge of the wound of inoculation and in general finds the artificial disease so mild that it hardly calls for help from any physician. This common-sense point of view was not shared by the majority of inoculators, in whose interest it was to emphasize the importance and gravity of the operation. But Mead's great influence and authority helps to smooth the path for the method. And indeed, all through the following years and considerably into the 19th century, we see variolation in England in continual progress. I need not enter into the details of its historic evolution here, since this has been admirably done by Creighton. It may be sufficient to point out that in the first 20 years of the revival, during which the method was exploited by more or less unscrupulous practitioners as a lucrative occupation, we do not find many evidences of a scientific improvement. In Kirkpatrick, Mead and Frewen we can already observe attempts at simplification and a desire for a better understanding of the fundamental questions involved. But it is only after 1764 with the advent of Gatti, the Suttons, Dimsdale, Watson, Mudge, Maty, Lettsom and others that a more scientific, systematic spirit is infused into the growing movement.

The tendency now becomes manifest to "prepare" chiefly by hygienic and dietetic means and to abandon frequent bleedings and violent purgation. The Suttons[50] have certainly a great share in the vulgarization of this practice. The mystery with which they surrounded their method and their successful avoidance of accidents were powerful factors in their favor. Their hygiene consisted mainly in a continuous open-air life before inoculation and during convalescence, to which were joined cold water applications. The secret remedies which they administered played probably an inferior rôle in the régime, though in popular belief they were assigned an important position. Their analysis (Ruston) showed them to contain the ingredients of Boerhaave's antidote (calomel and aethiops mineralis) and of the popular preventive pills of Schulz and others (colocynth, aloes, cloves, etc.).

Of greater importance in Daniel Sutton's régime were probably the attempts at attenuation of the virus itself and, in this regard, he probably learned from others, from Kirkpatrick and especially from Gatti, although it cannot be doubted that he himself was a capable observer and experimenter.[51] Attenuation of the virus was to be obtained in various ways: first by passing it through several human subjects (Kirkpatrick's arm-to-arm method),[52] by inoculating very small quantities of the virus and particularly by choosing it at the proper moment of development (the crude, unripe stage). We find all these points already suggested in Kirkpatrick's Charleston essay and, in passing, we may mention that Beddoes had tried to attenuate the virus by dilution with water, Woensel by mixing calomel with it, Kirkpatrick proposing camphor and other "scents."[53]

These efforts were all in the right direction, only it

[48] This hospital changed its location several times shortly after its opening in Windmill Street, to Mortimer Street and finally to Lower Street, Islington. The other hospital soon after opened at Bethnal Green (44 beds). After 1750 15 patients could be received, prepared and inoculated at the Inoculation Hospital in Old Street, St. Luke's, whence they were taken for after-treatment to the hospital at Fray Lane. In 1752 the governors of Charity opened another large smallpox hospital at Coldbath Fields (130 beds) also for preparation previous to inoculation.

[49] I do not find this delightful biting satire mentioned in any history of inoculation and it well deserves notice as it gives an invaluable picture of the manner of thought among certain physicians of the day. The author, it may well be Kirkpatrick, pretends that he is trying to expose "the low Absurdity, or Malice, of a late spurious Pamphlet, falsely ascribed" to Dr. Dod, and aims particularly at his principal case in physic: "giving an account of a person who was inoculated for the smallpox, and had the smallpox on the inoculation, and yet had it again." With banter and derision, jeering and sarcasm, he parodies Dod's bungling, awkward language, denounces his absurd reasonings and faulty observations. (In the Surgeon-General's Catalogue the author is given as W. Barrowby.)

[50] Of Robert Sutton we hear already in 1753 as an inoculator in Suffolk, where he experiments on himself and soon starts the business with three sons and a son-in-law, Dr. Hewit. Ten years afterwards his eldest son leaves him and begins on his own account at Ingatestone near Chelmsford (Essex), where he opens a hospital for inoculation and starts a flourishing enterprise with ramifications all over Great Britain and the Continent; his partner and assistants were Peale, Worlok, Sutherland and others.

[51] George Baker in 1766 tells us of Sutton's attempts at inoculating measles with the conjunctival fluid of patients.

[52] Thomas Frewen and others had already inoculated by this method in 1749 and abandoned Nettleton's deep incisions. Sutton seems to have avoided the virus from smallpox cases altogether.

[53] The admixture of musk to the virus practised by the Chinese may have had a similar motive.

appeared, particularly after Dimsdale[54] legitimized Sutton's method, that the attenuation was often carried so far that the result of the inoculation was sufficient to confer the desired immunity. Hence examples of relapses were cited and Bromfeild[55] had a right to fear that inoculation might become disgraced.

Sutton, Dimsdale and the others who adopted the "new method" did away effectually with the deep incisions, inaugurated by Nettleton and defended with so much tenacity. Slight punctures or scratches were now found to be amply sufficient and the disagreeable after treatment of the wounds was thus prevented. Tronchin introduced the virus into an artificial blister, a method followed extensively on the Continent and also intended to avoid the prolonged suppuration of the wound. This found little favor in England.

Thus the operation had reached a degree of simplicity, and lessened discomfort and danger, not thought possible before. Only the question of the protective value remained open. We remember that vaccination passed through similar phases and that relatively very late the necessity of re-vaccination became apparent. The test of repeated inoculations was resorted to quite frequently; we find reports of it all through the literature of those days. But experiments were also made to determine which part of the new régime and what kind of virus guaranteed the success of the operation. Watson,[56] who was physician at the Foundling Hospital where all children were inoculated, made some interesting experiments in 1767. Gatti was at that time in London and saw Watson often, which makes it very probable that he played some active part in them. Watson chose three parallel series of cases, 31 were inoculated with the virus from a smallpox case in the ichorous or watery state, 23 from another inoculated patient, but in the purulent state, and 20 others also from artificial smallpox with virus "in perfectly concocted state." This latter series was not "prepared" before inoculation, while the others went through the customary dietetic preparation (10 of the first series with calomel before and after inoculation). All of the patients were "out in the fields during the whole process." Watson gives a careful analysis of the results observed, some even in tabulated form, from which, as he puts it, every person is at liberty to make such deductions as he may think they will admit of. His personal conclusion is that the choice of the virus is not very material, that the ichor gives slightly better results, that the mercury has no specific effect and only acts favorably as a mild purgative. A well regulated vegetable diet before and during the whole process, the avoidance of heated rooms and heating liquors, he believes to be advantageous but not essential.

Re-inoculation experiments were undertaken by John Mudge[57] of Plymouth. Forty inoculations were made and seemed to demonstrate that "crude" matter taken from inoculation vesicles five days old does not convey immunity against a re-infection with natural or inoculated virus.

It is not evident that the results of these and other experiments exerted any revolutionizing influence on the method used earlier, but they must have helped towards perfecting it. The operation as then practised seems to have given satisfaction, for inoculations certainly became very popular in England, so much so that vaccination, in spite of the advantages which to us seem very clear, had first to subdue variolation before it could make any appreciable headway. It took exactly 44 years after Jenner's first vaccination, when, by act of Parliament, variolation was declared a felony.

Throughout this stage of evolution the Continent of Europe, in matters of variolation, is influenced by England. We see physicians arrive in London from various parts of Europe to study the method and on the other hand professional English inoculators travel all over the Continent to perform the operation, helping thereby its introduction.[58] Nowhere, however, did the practice reach the extent it had in England, although there is more noise about it and publications abound. This is a curious and notable fact, particularly when one considers that vaccination later was taken up in some continental countries more immediately and readily than in England. The first insistent plea for the introduction of variolation to the Continent was made by Voltaire from England where during his three years sojourn (after 1726) he had heard it discussed and had seen it practised in that country. That friend of John Locke's, Lord Peterborough, who, as we have seen, had brought Eller from Paris to London, took him also to his house. Voltaire made himself acquainted with everybody and everything with that eagerness so characteristic of him. Inoculation was on the wane just then, but its fundamental importance did not escape his keen mind. One of the many letters addressed to Theriot from England[59] is devoted to the subject of "l'insertion de la petite vérole." It is a most eloquent appeal. Motives common to all people, maternal tenderness and selfish interest,[60] he says, introduced inoculation to the Circassians. Then, by experience and observation of the disease and its peculiarities, this primitive people gradually evolves the idea of protective inoculation. How much more

[54] Thomas Dimsdale, 1712-1800.

[55] William Bromfeild, 1712-1792.

[56] William Watson, 1715-1787.

[57] For details the original ought to be consulted, also Creighton *op. cit.*, pp. 501 and 502.

[58] See Ebstein (*op. cit.*) about inoculations by George Motherby in Koenigsberg; Seitz about Baylies in Germany in Arch. d. Gesch. d. Med. II, 410; Chais (*op. cit.*) about Sutherland in Holland; Gardane (*op cit.*) about Worlok and Seeby in France; Power (*op. cit.*) also in France.

[59] "Lettres philosophiques," at first called "Lettres sur les Anglais." Letter IX written in 1727 and also published in "Dictionnaire Philosophique," 1764.

[60] The Circassian and Georgian beauties were much in demand for the Turkish harems. Voltaire found the story of the Circassian origin of inoculation in de la Motraye's Voyages, etc., La Haye, 1727. Later travellers in the Caucasus found nowhere signs of inoculation being practised there. Creighton waxes indignant about this "myth constructed in cold blood." He thinks it is given "as a mere assertion in the manner of a *philosophe*" and therefore needs no refutation, whereupon he proceeds to give a long one. Evidently he is not Voltaire's friend. (Creighton, *op. cit.*, II, 473, note.)

can an advanced nation profit from this by perfecting the method! And Voltaire did not, after the manner of some *philosophes*, stop with this one dramatic appeal. We find that through his life he continues to exert his influence in favor of the method. Thus it was he who persuaded Catherine the Great, of Russia, to undergo the operation. Dimsdale was called (1768) and also inoculated the Grand Duke Paul and many nobles and others in St. Petersburg and Moscow. Returning he left in his wake an inoculation hospital here and indirectly one other in Irkutsk, Siberia! Indeed an evidence of Voltaire's far-reaching influence!

France was, however, not yet ready for inoculation. Only 20 years later did it receive a general consideration. The reason for this is not very easy to understand. De Mariveaux in a reply to that letter of Voltaire's explained it thus: *si nous n'inoculons pas en France comme en Angleterre, c'est parce que les Anglais se décident par le calcul, et nous par le sentiment.* Whatever the reasons may have been, the fact remains and we know only of isolated trials, principally in Paris. We must note here one serious effort which seems to have escaped most historians. Tenon, the excellent surgeon of the Salpétrière, on his return from the campaign in Flanders (1745), quietly establishes an inoculation service in special premises annexed to the hospital. His interest in inoculation becomes evident only 10 years later when he inoculates the Comte de Châtelux, who in turn becomes an ardent champion of the cause. While Frenchmen on the whole were indifferent to the English example, the little republic of Geneva [61] had among its citizens men who evinced a distinct interest for everything English. Thus it may be explained how very early and determined efforts to introduce inoculation were made there. Already in 1748, Tronchin,[62] a Genevese settled for some years in Amsterdam, the favorite pupil of the old Boerhaave, had inoculated first his own son and then continued the practice among his patients. He introduced it also to Geneva where, on a visit in the summer of 1749, he inoculated a nephew, the son of the philosopher and magistrate Colandrini. Then the surgeon Guyot began to inoculate in September, 1750, and was soon followed by two physicians, Cramer and Joly. Trembley, the naturalist, another Genevese, had seen inoculations done in England and on the occasion of a visit to his home he suggested experiments in the hospital which were undertaken with encouraging results. In 1752 Guyot could report to Paris on his first 33 cases and others give accounts of even more, among them Buttini, who publishes an excellent essay. The practice is in full swing when Tronchin returns to Geneva (1754) and strangers flock into the town to be inoculated. In neighboring Lausanne Tissot,[63] who is already enjoying considerable fame as a practitioner, has taken up inoculation and publishes, in 1754, a treatise which was to be one of the most read and quoted in all Europe. Tissot's warm friend in Berne, the great Haller, has his own daughter inoculated and becomes active in its recommendation. J. Bernoulli does the same in Bâle and gives an address on the subject at the University. Mieg in the same town, S. Schinz and I. K. Rahn in Zurich, report on their results, but nowhere in this country we now call Switzerland does inoculation flourish as in Geneva, and it is here that it is carried to its logical consequences on a smaller scale but to the same effect as in England.

Two other countries, parts of what is now Germany and Sweden, also obtained their inspirations in the matter of variolation from England. Hanover, belonging to the English Crown, saw the first inoculations, as already told. Haller was in Göttingen from 1736 to 1753. There had been a little stir about inoculation in Hanover nearly 12 years before he arrived, when Maitland came to operate on Prince Frederick and Wreden had published his *Vernünftige Gedanken*. But those events were forgotten and Haller had more pressing things to attend to during his stay. That he took an active interest in the subject becomes evident a few years after his return to Berne in 1753. Another great man, Haller's friend Werlhoff,[64] at Hanover, was present at the inoculation of three other English princes in 1754, and from then on continued to inoculate together with Berger and others. Zimmermann,[65] who in 1768 replaced Werlhoff on the recommendation of Tissot and Haller, kept up an interest in inoculation. Murray,[66] in touch with England (Pringle) and Sweden (Schulz), writes excellent pleas. At Göttingen several inaugural dissertations were devoted to the subject (Grimmann, Houth and others under Schröder) after Roederer,[67] Haller's successor, had shown the way. Wrisberg,[68] the eminent anatomist, devised a special instrument, by which the depth of the incision could be regulated and we see later his great pupil, Soemmerring, as one of the earliest and most earnest supporters of vaccination. I have already referred to the English itinerant inoculators. At all the many little courts of Germany we see them appearing. Baylies [69] seems to have been the most active. His advent marks the introduction of the Suttonian method in Germany (announced by Wichmann in Hanover). Between 1767 and 1775 we can follow his tracks everywhere. Frederick the Great who, already in 1755, had expressed his astonishment that so little was done in Prussia for a promising method, calls Baylies to Berlin in 1775. He is to teach 14 physicians from the provinces his method in the hospital. We have notes on this course made by one of the physicians and from them it does not appear that the teacher had anything new to teach. Bay-

[61] L. Gautier, La Médecine à Genève, 1906, p. 391. Gautier gives in this interesting medical history a full account of the progress of inoculation in Geneva.

[62] Theodore Tronchin, 1709-1781; see his biography by H. Tronchin, Par. 1906.

[63] S. A. A. D. Tissot, 1728-1797, one of the most famous practitioners and prolific writers of the 18th century.

[64] P. G. Werlhoff, 1699-1767.

[65] J. G. Zimmermann, 1728-1795.

[66] J. A. M. Murray, 1740-1797.

[67] J. G. Roederer, 1726-1763.

[68] H. A. Wrisberg, 1739-1808.

[69] Will. Baylies of Bath, 1724-1789.

lies had a dispute with Muzel, who, with the elder Meckel,[70] had inoculated some persons several years before with very poor results, and this was probably the cause of his rather sudden departure. Other eminent men, Pastor Süssmilch,[71] the founder of medical statistics, and Möhsen in Berlin, Ludwig in Leipzig,[72] Tralles[73] in Breslau, Hensler,[74] the medical historian, and Juncker[75] in a special *Archiv*, plead the cause of inoculation, but these are all isolated instances without any marked practical results, reflecting the political chaos which was only very gradually focussing itself into a national unit. Only during the last decade of the century do inoculations become more numerous (Juncker) but these are soon given up in favor of vaccination.

In Sweden and Denmark also we see influences carried directly from England and Hanover. Of the progress in Sweden, Murray gives an excellent account and from Denmark Callisen[76] is able to report numerous inoculations. In both countries it is introduced at about the same time (1754 to 1756); in Sweden by a personal plea of the King on the advice of the medical college and the support of eminent men, among whom must be named Rosèn, Bergius and Schulz,[77] the latter publishing one of the best treatises on variolation. By the initiative of these men Sweden was receiving very early the benefits of an excellent medical and sanitary organization and inoculation benefits by it. Already in 1757 we see inoculation hospitals (Gotenborg) founded and we learn from a letter of Baron Scheffer to la Condamine that systematic inoculations in the public schools of Stockholm are undertaken. In Copenhagen also an inoculation hospital is founded, after Baroness Bernsdorff, probably on the suggestion of Berger of Hanover, her physician, had submitted her children to the operation.

Tronchin's first inoculation did not immediately create a following in Holland. Only six years afterwards, in the year (1754), when he was leaving the country, we hear of the first inoculation performed by a Dutchman,[78] the excellent anatomist, Thomas Schwencke, at The Hague. In the same town inoculation finds an ardent defender in Pastor Chais and one of its most formidable opponents, Anton de Haën, who, however, is just leaving The Hague to go to Vienna. Thanks to the efforts of influential scientific men like Hovius and Camper[79] in Amsterdam, the interest in variolation is preserved and even carried to the Dutch Indies.[80]

[70] J. F. Meckel, 1714-1774.

[71] J. P. Süssmilch, 1707-1767.

[72] Chr. G. Ludwig, 1709-1773. Among his many writings is one of peculiar interest in regard to the study of medicine, *De medicinae studio non praecipitando*, 1772.

[73] B. L. Tralles, 1708-1797.

[74] P. G. Hensler, 1733-1805.

[75] J. C. W. Juncker, 1761-1800.

[76] H. Callisen, 1740-1824.

[77] Nils Rosèn (von Rosenstein), 1706-1773. P. J. Bergius, 1730-1790. Dav. Schulz (von Schulzenheim), 1732-1823.

[78] Van Leersum's account of inoculation in Holland in Janus, 1910, XV, 363.

[79] Jacob Hovius, 1710-1786; Petrus Camper, 1722-1789.

[80] van Hogendorp, v. d. Steeg, van Nielen (Batavia), *op. cit.*

The greatness of Dutch medicine slowly vanishes after the death of Boerhaave. Van Swieten[81] rapidly transplants the spirit of the Leyden school to Vienna. To count Van Swieten as one of the opponents to inoculation as is often done is not correct. We find him writing on July 23, 1755, to Dr. van Leempoel[82] from Vienna: "I am in favor of inoculation —and endeavor to introduce it here," and again in February, 1757, to de la Condamine that he is waiting for spring to begin experiments with it. It is not certain that these trials were then made, but we do know that later on experiments were certainly made with his consent and interested attention. The truth of the matter probably is that he kept above all parties. De Haën[83] on the contrary, soon after his arrival in Vienna, proclaimed his sweeping condemnation of inoculation. In 1759, in his "Questiones," he asks: "Is inoculation permissible before God? Will inoculated smallpox spare more people's lives than the natural disease? Is it really true that almost everyone must get the smallpox? Is it not doubtful whether inoculation, after conveying the disease or not, protects against a new attack?" All these questions de Haën answered emphatically in the negative, but with little solid substantiation. His ruthless attack on the promoters of variolation caused a literary stir. Tralles in Breslau, Tissot in Lausanne and de la Condamine in Paris answered by letters which really were treatises. De Haën thereupon pronounced a summary "refutation" of inoculation. His character is extremely difficult to understand, but as a teacher of great merit he undoubtedly helped Van Swieten in the reorganization of the medical school, thereby establishing its fame. Though ultraconservative, still interested in processes against witchcraft, which explains his interest in the moral side of inoculation, he was one of the first to utilize the thermometer clinically, while percussion, or Haller's teaching, did not interest him. His bark, however, must have been worse than his bite for he does not seem to stem the incoming tide of inoculation in Vienna. The Empress Maria Theresa, 50 years old, having recovered from smallpox, in 1767, on the recommendation of Pringle, calls Jan Ingen-Housz, a Dutch pupil of Dimsdale's to Vienna for the inoculation of two archdukes and one archduchess. The satisfactory result of the operation, after an extensive series of 200 test cases, opens the doors wide to the practice, which, particularly at the hands of Stoerck[84] and Locher, receives a thorough application and investigation. We have an excellent account of this period of inoculation in Vienna by Rechberger.

It remains now to review the subsequent fate of variolation in Paris, and in France and those countries more directly inspired from there. Paris was then, even more than it is now, the center of all activities in France and therefore it must appear strange that the most important local developments in regard to inoculation issued from two strangers, Tronchin and

[81] Gerard van Swieten, 1700-1772.

[82] Janus, 1910, XV, 368 (van Leersum).

[83] Anton de Haën, 1704-1776.

[84] Anton Frhr. von Stoerck, 1731-1803.

Gatti. When Gatti[85] appeared in Paris from his home in Pisa in 1760 he found, as he expressed it, "more brochures for and against inoculation than inoculations." This must have been very near the truth all through the whole period of variolation in France, for nowhere do we find anything approaching the number of inoculations reported in England, while we have to make our way through innumerable books, letters, pamphlets, fugitive leaves, etc., in order to get at the actual facts. Plentiful ideas are exposed with characteristic vivacity and sprightliness but reports of actual experiments are meager. When they do occur they almost always evince clear and penetrating observations. The war of pamphlets began in 1754, when de la Condamine[86] returned from a voyage of exploration in South America, whence he brought back the exact measurements of an equatorial degree, cinchona bark, rubber and, what interests us most, a deep conviction of the value of inoculation. A Carmelite missionary in Para had seen something in a European gazette about inoculation and, smallpox being in evidence, he at once inoculated his flock with excellent results. De la Condamine had seen him and his experiments and became convinced. He had no medical training, his leaning was towards mathematics and he had entered the Academy of Sciences, as he puts it, by the door of chemistry, the only one open. On April 24, 1754, a memorable day in the French annals of variolation, he addresses, for the first time, the Academy in favor of inoculation. His plea is based almost entirely on the English experiences as given in Kirkpatrick's "analysis" and some later publications including the reports from Geneva. As an embellishment are used the picturesque details of the "Greek method." It is one of those speeches the like of which we have often had occasion to hear in our own fight against the "white plague"; the danger is graphically described, the simplicity of the preventive means outlined, and the results to be achieved are mathematically fixed. "If inoculation had been introduced into France in 1723," concludes de la Condamine, "we would now have saved the lives of about one million people without counting their offspring." The effect of this address was that it stirred up great interest in inoculation. When one now reads the literature on inoculation which followed de la Condamine's *mémoire*, one gets the impression that, almost up to the advent of Dr. Guillotin's little instrument, nothing interested the French so much as how to save lives either with or without inoculation. That is probably what de Mariveaux meant by French *sentiment* as against English *calcul!*

Actual experiments, however, were very scarce. People in general, even those who took de la Condamine's views of the matter, seemed deadly afraid of the operation. We hear of the inoculation of some children on the advice of Turgot, a young lawyer and later a powerful minister. The Marquis de Châtelux was the first adult to go through the still dreaded test.[87] An example from royalty was much needed. In almost every European court variolation had entered comparatively easily, probably because a preventive was most anxiously desired in those palaces crowded by a suite often numbering into the thousands and thus offering particular dangers. The Duke of Orleans, grandson of the Regent, who, by his death in 1723, had disappointed the early hopes of inoculators, was now determined to make the experiment in spite of small encouragement from Louis XV. A friend of Tronchin's, de Jancourt, probably persuaded him, and Sénac,[88] who only later became an opponent, approved of it. Tronchin arrives very quietly and the operation is performed towards the end of March on the two children, the Duke de Chartres and Mlle. de Montpensier, with the assistance of Hosty and Kirkpatrick. Everything goes well and Tronchin is the hero of the day. The psychology of this moment and the individuality of the principal actors are most interestingly analyzed in the biography of Tronchin[89] by one of his descendants, reviewed for American readers by Dr. F. C. Shattuck. Tronchin's stay in Paris was short, he departed in June, but it seems that during that time he performed a number of inoculations among the nobility. I am inclined to think that the number was very small and when the Duc de Luynes in his memoirs (March 28, 1756) says: "Tronchin pretends to have inoculated 20,000 persons," someone is grossly exaggerating. From Tronchin, who was not given to writing, we have no direct expression, but Roux, an eye-witness, gives (1765) a most interesting description of the whole method of treatment as carried out in the house Tronchin had hired for the purpose of receiving his patients for inoculation. They were "prepared" for it by a dietetic régime of one month. In the particular case cited by Roux 26 days were required from the time of inoculation to the final discharge, and 10 more for the healing of the wound. There were some rather alarming symptoms in this case and de l'Epine, referring to it later, thinks it was as bad as the real smallpox, but Tronchin, in a letter to Morel (1767), says that the patients treated by his method in Paris were less ill than those treated by the old method.[90] One really cannot wonder that people did not take to the old method and greeted the coming of Gatti a few years later (1760). He indeed brought simplification and perhaps went too far in the opposite direction, as some of his failures seem to indicate. Gatti hails from Pisa where he held the chair of medicine at the university. He was brought

[85] Angelo Gatti of Mugello (Tuscany) was professor of medicine in Pisa.

[86] De la Condamine, 1701-1774. He had already, once before, in 1732, attempted to interest the Academy in inoculation but failed.

[87] Buffon's words, when addressing de Châtelux at his reception to the French Academy in 1775, are: "Alone, without advice, in the flower of your youth, but decided by a maturity of reason, you went through the test then still dreaded."

[88] Jean-Baptiste Sénac, 1693-1770.

[89] H. Tronchin: Un médecin du XVIII siècle, Theodore Tronchin (1709-1781), Paris, 1906, Plon 8°. See also F. C. Shattuck in Boston Med. and Surg. J., 1908, CLIX, 1-5. A less favorable judgment of Tronchin is to be found in a paper by A. Geyl, based on Dutch documents (Arch. f. Gesch. d. Med., 1908, 1, 81, *et seq.*).

[90] This case of Tronchin's as reported by Roux (1765) offers so good an illustration of the method as then practised, that an

to Paris by his friend Baron d'Holbach[91] and inoculated his children. Well introduced, he immediately found a great following. In 1763, 1764 and 1767 he publishes his ideas and the developments and results of his method in a direct and frank manner, which contrasted favorably with the mass of other writings. He co-operates with Roux, Antoine Petit, Bordeu[92] and others. His *réflexions* of 1764 particularly maintain a standpoint far in advance of his time. He sets out with a discussion of the etiology of smallpox. He objects to the lax conceptions then prevalent, expressed in vague terms of fermentation, ebullition, effervescence, humors, leaven, germ, etc. They mean nothing. Variola is always produced by the action of a foreign body introduced into the organism from the outside, by contagion or other communication. It is the constant and determinate effect of a specific "virus," which reproduces itself and multiplies. He insists especially on the specificity. Communication of the disease takes place through contact, inhalation or ingestion. These were revolutionary views then, and to-day we do not know much more about variola. By inoculation, he goes on, the poison is conveyed by intelligence, in the natural disease by chance. A preparation of a subject for inoculation has sense only if it tends to improve his general health; debilitating measures like bleeding and purging, as practised by routine even on feeble individuals, have sometimes brought tears of pity and indignation to his eyes. As to the choice of the virus it is of lesser moment whether it is "crude," or "mature"; the important factor is that the individual from whom it is derived be in good general health and free from other contagious disease.[93] It is best to obtain the virus from another inoculation and he replies to the objection made, that the virus becomes hereby weakened: "There would be nothing left to desire in the art of inoculation, if we could arrive at attenuating the variolous virus, but I do not know any means by which this attenuation can be accomplished."[94] The passage of the virus through several organisms may in time bring about a marked decrease of virulence and he adds prophetically: "Perhaps one day we may become indebted to inoculation for having brought about an attenuation of this poison among men." It is of no advantage to try and produce an abundant crop of pustules, *one* well developed pustule has as much protective value as a thousand. In case of doubt re-inoculation ought to be resorted to. With great vehemence Gatti turns against the unscrupulous practitioners, who, for selfish reasons, surround the method with all sorts of complicated details; he proclaims it a very simple operation and its chief principles are a thorough knowledge of the patient's condition and the art not to do harm, *partie la plus fine et la plus importante de la médecine.* He believes also that women could be instructed to the best advantage in the practice of inoculation. Gatti is absolutely convinced of the protective power of inoculated smallpox. He even substantiates this belief later by offering a considerable money prize for any authenticated case of re-infection after inoculation. Such cases, he thinks, can only happen when the eruption after inoculation is not one of true smallpox but is mistaken for it (he alludes here to chickenpox). He admits to have been deceived himself. The celebrated case of the Duchesse de Boufflers, illustrating such an instance, hurt Gatti's cause more than any other.[95]

After a careful consideration of Gatti's work and its proper

extract may prove interesting: The patient is the son of d'Héricourt (*intendant de la marine*), 12 years old, delicate, anemic.

13. March 1756 régime begins, one-half of ordinary diet, chiefly farinaceous, some veal, mutton, chicken and vegetables. Every night tepid foot bath for one-half hour.
10. April. Roux moves with the young man, his pupil since 6 years, to Tronchin's house, where they sleep together in same alcove.
11. April. Surgeon Saint-Martin applies vesicant to insides of both legs.
12. April. *Inoculation:* Blisters are opened, threads with virus applied.
13. April. Removal of threads, bandage with digestive ointment, continued next day.
18. April. Around each wound red circle, beginning excavation.
20. April. Patient uneasy, headache, inguinal glands swell. Up to here from day of inoculation only vegetables, soup and barley water allowed.
21. April. Glands sensitive and painful, *fever sets in* 9 a. m. slight.
22. April. Fever higher, at 7 p. m. slight delirium, all night and next day, papules on chest.
23. April. Slight delirium and fever until 7 p. m. In morning slight epistaxis. During this febrile and eruptive period only barley water allowed.
24. April. No fever, eruption finished, slight nose-bleed.
25. April. Papules grow in size rapidly, some paler. Sixty-six on face and as many on body, distinct and with red circles.
27. April. Suppuration of pustules, wounds which were almost dry and covered by brown scab, begin to suppurate abundantly.
28. April. Some pustules begin to dry up. Saint-Martin opens some to take virus on threads.
4. May. (22d day after inoculation.) Exsiccation complete. wounds discharge for 15 further days. During febrile period, diet same as before fever set in.
9. May. Slight "erysipelas" of face and around one leg, which continues for 3 to 4 days. "Patient subject to this." No fever. Roux calls this a benign case. He mentions by name seven other patients under the care of of Tronchin at the same time.

[91] P.-H.-T. d'Holbach, 1723-1789, of German origin, but settled in Paris. He achieved some fame as a sceptic philosopher and entertained at his table all the *bels esprits* of the day. Galiani called him the *premier maitre d'hôtel de la philosophie.*

[92] Théophile de Bordeu, 1722-1776.

[93] Gatti admits that other diseases than variola can be conveyed by inoculation; it has happened to him with scarlatina and measles. Consumption (*pulmonie*) he does not believe to be thus transferred.

[94] "*Je suis persuadé qu'il serait utile de pouvoir affaiblir la matière variolique, qu'il ne resterait plus rien à désirer dans l'art d'inoculer, si on pouvait y parvenir, mais que je ne connais aucun moyen d'obtenir cet affaiblissement.*"

[95] In the Gaz. litter. de l'Europe, Tome VI, p. 377 (also Gent. Magaz. Nov., 1765) is given a statement of the case by the Duchesse de Boufflers herself. It is widely discussed in France by de l'Epine, Ant. Petit and de Baux during the deliberations of the Faculty of Medicine. The best English account, with Gatti's explanations, is to be found in Langton, *op. cit.*, pp. 18-25. (Creighton gives an abstract in his book, II, 495.)

position in historical sequence, one is forced to the conclusion that the reformation which took place in the practice of inoculation during the sixties issued from him and that the success of Daniel Sutton and his followers is based on the methods advocated by Gatti. On the other hand it is evident that Gatti later on adopted some of the features of the Suttonian régime, notably the cold water applications and the open-air life. His adoption of the use of cold water is no blind imitation; it was based on the observation that whenever the fever, which usually follows the local eruption after three days, is delayed, the symptoms of the disease are lighter. By cold water applications he was able to delay the fever until the sixth day. But he makes no sweeping conclusions, he insists on further experiments and particularly on watching the relation of the local and general reaction.

The serious objection against inoculation, that of increasing the spread of the disease, Gatti frankly admits, but he believes that, since each infective focus is known, proper isolation could obviate any real danger. He seems, however, not to have been able to control all of his patients. That some of them had been seen to mix unhindered with others in public places was one of the chief causes of government interference. In a decree of Parliament, dated June 8, the General of Police alludes to the "murmurs of the Public" at the indiscretion of certain partisans of the method, which have "reached our ears." The "general cry" raised against the inoculators makes necessary an investigation by the enlightened magistrates. The *avocat du Roi,* Omer Joly de Fleury, then further enlarges on these reasons and concludes his address to the magistrates: "The fact of inoculation which now must fix your attention, presents itself naturally from two points of view, first as regards the principles of religion, secondly as regards the advantages humanity may derive therefrom." Experts in conscience and health will therefore have to be consulted. These of course are the Faculties of Theology and of Medicine respectively. The medical faculty is to give its advice first and then submit it to the theologians. The question of a continuation of a provisional tolerance to further "free literary discussion and various experiments" is set aside and it is decided to substitute for it a provisional prohibition against inoculating within the precincts of cities and suburbs until the named faculties have been able to recommend the permission, or prohibition, or tolerance of the practice.

From now on all inoculations have to be done outside the *barrières* and we see many go there, for the legally imposed limit of six weeks, to submit to inoculation. We know of numerous inoculations being performed under these restrictions by Gatti, Petit, Roux and others. Tronchin also sets up an establishment there in 1766 and Worlock,[86] the father-in-law of Sutton, and an assistant do the same.

Meanwhile the Faculty of Medicine goes to work on its report. A commission of twelve members is appointed and the procedure of investigation is outlined. This same faculty which long ago had approved, then condemned antimony, and rejected the discovery of the circulation, proposes to decide this question again on similar evidence. Not the slightest effort is made to adduce further experiments, only the literature is to be studied and the opinions which inoculators outside of Paris are asked to express. Regular meetings are held by the commission, partly in camera, partly before the assembled faculty, and tumultuous scenes occur in which parliamentary methods are forgotten and personal encounters are threatened. The commissioners soon found they could not agree and decided to present two reports instead of one. Two groups of six each were formed, one, of those in favor, led by Petit, the other, of those against inoculation, headed by de l'Epine.[87] The former represented the younger, more progressive, the latter the older, conservative elements. Only 15 months after the parliamentary decree could the reports be presented before the assembled faculty for the first reading and, after acceptance, be put into the printer's hands. The publication, however, was delayed until 1766 and supplements were added as late as 1767. The report of de l'Épine would do honor to any prosecuting attorney; as such it is a very clever presentation of the case against inoculation. It occupies 125 quarto pages, mostly filled by the bibliographic reviews of the literature in fine print.[88] The main points are that smallpox is not so dangerous a disease as is usually asserted. De Haën had treated 120 cases with only five deaths, which may be explained as due to other causes. Bad treatment is at the bottom of most deaths. Furthermore many people never get smallpox and a fatal inoculation might strike just those. One such case is enough to condemn inoculation. Much is made of one of Gatti's failures and of the Boston reports (Delahonde) of an increase of smallpox following inoculation. In conclusion an attempt is made to show that the provisional prohibition has had already a favorable influence on the general health in Paris and "one begins to breathe again. The epidemic, no longer nourished and perpetuated by this unfortunate practice, has lost much of its force and is notably diminished."[89]

De l'Épine in his closing remarks suggests that the method

[86] Gardane, *Secret des Suttons.*

[87] The other commissioners in favor of inoculation with Antoine Petit were E. L. Geoffroy, A. C. Lorry, Maloët, Thiery and Cochu, while the opponents under G. J. de l'Epine's lead were, Jean Astruc, M. P. Bouvart, Th. Baron, J. Verdelhan de Miles and H. J. Mocquart.

[88] Three separate sessions of the faculty were needed for the reading of this part of the report, viz., Oct. 20, 22 and 24, 1764.

[89] The summary of the conclusions is given in "nine incontestable truths" as follows:

1. Incertitude of conveying smallpox by inoculation, even if repeated.
2. Unsuccessful inoculation does not protect in future.
3. If successful there is no guarantee that attack will be benign.
4. If death is not issue, frequent disturbances may follow.
5. Same risks as in natural smallpox, disfiguration, etc.
6. Escape from death after inoculation insures no protection against other often more dangerous attacks.
7. Other diseases may be conveyed through inoculation.
8. Inoculated smallpox is sometimes fatal.
9. It can infect others and thus endanger society.

is perhaps not sufficiently perfected and hopes that the English may succeed, then "we shall thank heaven for such a precious discovery and we shall render them due homage for the enlightenment which they have procured for us at their risk. It would be unjust for us to envy them the very legitimate advantage of enjoying the first fruits, reaped under such perilous circumstances." The inevitable advice of these six commissioners is neither to permit nor to tolerate inoculation.

Of the signers of this verdict Astruc [100] was undoubtedly the most famous and influential. Eighty years old and only two years before his death, it cannot be presumed, however, that he took a very active part in the composition of this report. Bouvart,[101] another member, we can safely make responsible for several of the more extreme attacks against the inoculators. He was a violent antagonist of Tronchin's, whose book on the colic of Poitou he had tried to drown under a flood of ridicule and unjust criticism, and with Petit, the editor of the other report, he had had a quarrel about the very important question of belated childbirth.[102]

The report of the other party, edited by Petit,[103] is not nearly as carefully prepared as the de l'Épine document. One feels that it is written by a busy practitioner who has little time and inclination to enter into all the subtleties introduced. He judges from what he has seen, simply brushing aside the objections. It is not nearly as convincing for the casual reader as the other, in which almost all the reports of inoculators are dexterously turned against themselves, thus exhibiting a formidable array of damaging testimony. Petit did not follow such tactics in his first report, but, seeing that he had failed to make an impression, comes out in 1766 with a second report in which he shows the malice of de l'Épine's method. He points out the "multiple errors and mistakes of all sorts" and these become evident enough when one compares them with the sources.

This second report is signed by only three of the commissioners besides Petit, viz., Geoffroy, Lorry and Maloët,[104] the other two are absent and the Doyen Belleteste and the censor Le Thieullier therefore sign in their stead.

The endless discussions[105] about the merits of inoculation during these several years must have exhausted the interest in the subject and indeed, after the assembled faculty had expressed itself in favor of the tolerance of inoculation under certain restrictions by 52 votes against 26, we hear little more on the subject. Petit, in a later letter to the Doyen of the Faculty, thinks that, up to the end of 1766, probably 15,000 inoculations had been performed in France, which seems little against the 200,000 reported from England. Although the acuteness of popular interest[106] had subsided, we have good reason to assume that inoculation was continued in Paris and the provinces on a much larger scale. We have, however, no evidence that anything was done, as in England, to further study and develop the method.[107] We should naturally expect to hear of Gatti's further work, but there is very little to be found about him. In 1769 he receives permission to inoculate in the military college, but of his results and the details of his work I have been unable to detect traces. Louis XV dies of smallpox in 1774 and this event decides his grandson and successor, Louis XVI, to submit himself as well as his family to inoculation. Neither with Louis XV's illness nor with this inoculation do we find Gatti's name connected, although he was physician extraordinary to the King.[108] Gatti's appearance and activity marks the greatest advance in variolation which was reached in France and, as a matter of fact, anywhere. His ideas and methods were those of the best scientists at the end of the 19th century and it is indeed remarkable how little his work is remembered.[109]

In England, and to some extent also on the Continent, after the technical principles of variolation became fairly well understood, we can see developing round it a social movement for the eradication of smallpox very similar to the tuberculosis crusade of our days. I have already alluded to the hygienic features in the regimen; they were enlarged upon and generalized for a wider application. Segregation of the infected cases was insisted upon more strongly than before. Early inoculation of infants was advocated by Maty and more emphatically by Lettsom. The demands for inoculation dispensaries became very loud and several were established (John Clark at Newcastle, Haygarth at Chester, etc.). The number of inoculations practised was exceedingly great. It went to many thousands per year. We have, of course, no accurate reports about it. But already in 1766 (Houlton) we hear that

[100] Jean Astruc, 1684-1766.

[101] M.-P. Bouvart, 1717-1787.

[102] The contention was about the legitimacy of a child born after an 11½ months pregnancy and 10½ months after the death of the 76-year-old father.

[103] Antoine Petit. 1718-1794.

[104] Etienne-Louis Geoffroy, 1725-1810, for 40 years one of the most prominent Paris physicians; Anne-Charles Lorry 1726-1786, good observer and medical historian of merit; P. L. Maloët, 1730-1810, able practitioner.

[105] Dubourg, *op. cit.*

[106] John Wilkes during his exile in Paris seems to have become interested in inoculation to the extent of writing a farce about it (*op. cit.*).

[107] The principal clinical reports of this time, besides the ones already cited, are those of Robert, Rast, Grassot, Rasoux, Dezoteux, Le Camus, Gardane, Gandoger de Foigny, Mangin, Vernage (*op. cit.*). Théophile de Bordeu, the founder of the theory of "vitalism" publishes (*op. cit.*), in defence of inoculation, a long historical treatise, in which he analyses what attitude the founders of all the medical doctrines since Hippocrates might have assumed in regard to inoculation.

[108] Report by de Lassone (*op. cit.*).

[109] In his own country, Italy, he does not seem to have exerted any great influence in favor of variolation. The considerable development which it reached there was inspired chiefly from France, Switzerland and Austria. The personal initiative of the Marchese Bufalini in Rome in 1754, the opposition of the Papal physician, Zanettini, and of Dr. Roncalli Parolino, and Tronchin's inoculation of a Bourbon prince in Parma are the main events of the Italian history of variolation. The most active Italian inoculators were Peverini, Lunadei, Lavizzari, Caluri, Targione, Manetti, Berzi, Bicetti (*op. cit.*). In Spain there seems to have been only a literary reflex of the French efforts.

Robert Sutton had inoculated 2514 persons from 1757 to 1767 and Daniel 13,792 from 1764 to 1766 and his assistants 6000 more.[119] As late as 1821 to 1822 John Forbes tells us that a farmer, Pearce and son, of Busham (Sussex) associated with some surgeons inoculated 13,000 persons!

Jenner's (born in 1749) interest in the subject dates from this period. John Hunter had told him already not to speculate but to observe and prove. With his natural gifts, with the inspiration of that particular period and the opportunities of his home surroundings it was inevitable that he should make the greatest improvement in the method of inoculation.

In following variolation on its course through the civilized world of the 18th century and, in noting the successive steps of its evolution, it has been my aim rather to open avenues for future research than to give a complete and detailed account of the more important phases. Plentiful suggestions are to be found everywhere which lead one to infer that variolation, without the advent of vaccination, might have furnished the world with an equally safe and perhaps more efficient method of preventive immunization. We have every reason, however, to be satisfied with the results of vaccination. Thanks to it smallpox has been practically stricken off the list of the great medical problems. None the less it is time that the epoch which preceded vaccination should receive its proper place in the history of medicine, and that the names of Kirkpatrick, Gatti, Watson, Mudge and Dimsdale should be recalled with that of Edward Jenner.

[119] His income for 1764 is given as £2200 and for 1765 as £6300.

A full bibliography on variolation (over 600 items) has been collected by the author and is arranged under the headings: 18th Century, Americana and modern literature. It will appear in the reprints which Dr. Kleb's will be pleased to send anybody who will write to him.

LECTURES ON THE HERTER FOUNDATION.

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LECTURE II.

TRYPANOSOMIASIS.

The term trypanosomiasis is applied to-day to a group of diseases affecting vertebrates and caused by parasitic protozoa belonging to the family Trypanosomidae. These parasites occur chiefly in the blood plasma and the typical form possesses an elongated body, an undulating membrane, a single nucleus, a blepharoplast, and a chromatic filament running along its length from near the blepharoplast, along the margin of the undulating membrane, to terminate freely at one end of the body. The latter has a somewhat spiral form, the protoplasm being alveolar and at times showing a granular structure. An axial filament has been described as occurring in some forms. One species, *Trypanosoma equiperdum*, occurs largely in the lymph, and another, *T. gambiense*, may invade the cerebrospinal fluid. They are actively motile organisms, multiplying usually by longitudinal or multiple division. Numerous species have been successfully cultivated in vitro in the presence of haemoglobin and by this means many trypanosomes have been discovered in animals in which these parasites occur in such scanty numbers that their presence cannot be detected microscopically. Thus a large percentage of birds and cattle in different parts of the world have been found to harbour trypanosomes in their blood.

It would appear from the evidence gathered of late years that the majority of these parasites are conveyed from host to host by blood-sucking ectoparasites, either arthropods or leeches, whereas in some cases there is clear proof (partly experimental) that infection may take place directly from vertebrate to vertebrate through the contact of abraded or even healthy mucous membranes and skin. Although much has been written regarding a supposed sexual phase in the life-cycle of trypanosomes, we are still in the dark as to its occurrence, the little evidence there is points, however, to its possible occurrence in the invertebrate hosts which serve as vectors, so that, at any rate provisionally, these may be regarded as the definitive hosts of the parasite. Infection may be brought about under experimental conditions by the inoculation of blood containing trypanosomes, or by applying blood to abraded or intact mucous membranes and skin. In nature, the infection of dogs by feeding on animals dead of surra (due to *T. evansi*) has frequently been observed, and similar results have been obtained experimentally. Dourine in horses is commonly communicated in nature in the act of coitus, and Koch suspected that the trypanosome of sleeping sickness (*T. gambiense*) might be similarly communicable in man, a supposition which has since been strengthened by laboratory experience. In one instance there is evidence that non-biting insects, *Musca domestica*, may serve as vectors; I refer to the equine disease "murrina" at Panama, due to *T. hippicum*, which is not apparently transmitted unless the animals show wounds of the skin upon which flies may alight and thus convey the parasites directly from host to host. In this case, also it is possible that infection may take place by coitus.

Judging from earlier evidence which proved that different species of trypanosomes could be readily communicated from animal to animal by inoculation, in some cases by the transference of minute quantities of blood, it was generally supposed that the parasites, under natural conditions, were communicated by biting flies in a purely mechanical manner. Experimental evidence on this point appeared, moreover, to bear out this supposition, for in a number of instances trypanosomes were transmitted from diseased to healthy animals by removing a fly from an infected animal upon which it was feeding and, soon after, transferring it to a healthy animal

upon which it was allowed to complete its meal. For a long time the classical experiments of Bruce, in Zululand,[1] were accepted as evidence of the mechanical transference of *T. brucei* by *Glossina morsitans* (Fig. 10), he having found that infected flies captured in nature did not infect healthy horses if the flies were prevented from feeding upon them for 24 hours or more after they had been captured. Although some authors, notably in India, still regard *mechanical* transference by biting flies (*Stomoxys, Tabanus, Culicidae*) as of importance in the spread of infection, the general trend of opinion to-day is to regard such transference as possible, but of slight significance, in the epidemiology of trypanosomiasis.

Owing to the widespread interest evoked by recent advances in tropical medicine, a large number of observers in all parts of the world have devoted much attention to the study of microscopic parasites occurring in the blood of vertebrates. The result has been that we now know of a vast number of hosts which harbour trypanosomes in their blood, and the literature relating to new species of these haematozoa has grown to be one of considerable magnitude. The general tendency has been to consider each species of animal as the

FIG. 10.—*Glossina morsitans* Westwood.

carrier of a species of trypanosome peculiar to itself, this being doubtless due in part to the supposedly specific character of the adaptation shown by the parasite to its host. For a long time, one of the best known trypanosomes, *T. lewisi,* was regarded as peculiar to rats, and it is only recently that it has been shown to be also capable of living parasitically in other rodents. We know now that certain species of trypanosomes possess a wide range of pathogenicity, such forms as *T. brucei, T. gambiense, T. evansi,* and others being pathogenic for many different species of mammals. In some cases, morphological characters sufficiently differentiate the species, but our confidence in some of these characters has been shaken since we know that a species of trypanosome may alter its appearance in changing its host. Whereas the immunity reactions have been used to differentiate species of trypanosomes, a means of distinguishing species to which no zoölogist will agree, we now know that this means of differentiation cannot be relied upon since the virulence (an obscure character) of the parasites can be considerably modified experimentally.

Of the discoveries which have been made of recent years with regard to trypanosomiasis, those which concern the mode of infection by blood-sucking ectoparasites unquestionably spring into prominence both because of their great scientific interest and practical bearing upon preventive measures designed especially to protect man and the more valuable domesticated animals against trypanosome infections. Sleeping sickness and nagana in Africa are amongst the most deadly diseases known, and I shall commence by outlining what we know to-day regarding the way in which they are spread.

SLEEPING SICKNESS.

Trypanosoma gambiense, the cause of sleeping sickness in Uganda and the west coast of Africa, is conveyed by *Glossina palpalis.* It has been estimated that 0.03-0.34 per cent of wild *palpalis* in the endemic area in Uganda are infective. Infective flies have been captured on the shores of Lake Victoria Nyanza which have been uninhabited by man for three years and they have been found on islands from which the human population has been removed for 10 months. There is no evidence that *T. gambiense* is hereditarily transmitted to the offspring of an infected fly, and it cannot be assumed that *palpalis* in nature can live for any such period. We were, therefore, forced to conclude that animals inhabiting this region must be susceptible to infection and capable of harbouring the trypanosome. It is now definitely established that certain animals do serve as *"reservoirs"* whence the flies may derive the parasite in the absence of man. The latest reports prove that antelope (bush-buck, reed-buck and water-buck) may harbour the trypanosome in nature. Antelope kept under observation have been seen to recover from any clinical manifestations of the disease and to appear perfectly healthy for 12 to 22 months, but they continue to harbour *T. gambiense* during this period and possibly longer, and throughout this long interval of time they may, as has been experimentally shown, infect clean *palpalis* which have been raised in the laboratory. Although there is evidence that with time the antelope's blood grows less virulent, as tested by inoculation into susceptible animals, and that antelope acquire a form of immunity, they harbour virulent *gambiense* for a sufficient length of time to maintain the parasite in nature in the absence of man. As in other diseases, so with trypanosomiasis, it is the *chronic cases* which serve as "reservoirs" for lengthy periods, and are most dangerous in relation to the spread and persistence of the disease in the region affected. The relation of game animals in respect to sleeping sickness in man is, therefore, similar to that of game in relation to nagana in domesticated animals; in both cases game may serve as a reservoir whence the *Glossinas* draw their infection. The wide range of pathogenicity possessed by *T. gambiense* renders it certain that it must, in nature, find reservoirs in other animals than antelope. In fact, the trypanosome has been recovered from cattle, monkeys (*Cercopithecus,* twice) and dogs under natural conditions. A large series of animals has been proved to be susceptible to infection by inoculation with *T. gambiense* of human origin. Without, perhaps, giving an exhaustive list, I would mention that, in addition to the animals already noted, the chimpanzee, macacus, lemur, cat, pig, goat, sheep, hedgehog, mouse, rat, guinea-pig, rabbit, horse and donkey have been found susceptible to infection with *T. gambiense.*

On the other hand, birds, reptiles and amphibia appear to be immune. The parasite has been conveyed experimentally to susceptible animals either by flies captured in a wild state or by clean flies purposely infected in the laboratory. Monkeys, sheep, goats and the duiker-bok have been successfully infected in this manner.

Experiments carried out with *G. palpalis* in captivity have shown that but a limited number—about 5 to 6 per cent—become infective after feeding upon blood containing *T. gambiense*.[5] In such flies a certain number of trypanosomes always degenerate and die but others soon begin to multiply rapidly throughout the gut, and this multiplication has been seen to continue within the fly's gut up to the 95th day, being maintained by repeatedly feeding the fly upon clean blood. The trypanosomes disappear from the fly's proboscis very soon after the insect has partaken of infected blood. The parasites occur in a variety of forms within the gut, they have not been found in the coelomic cavity, and it is only after a period of 25-28 days following the infective meal that they appear in the salivary glands of the insect. During the few hours immediately following an infective meal, the fly may transmit the trypanosome, this being doubtless due to parasites ejected from the proboscis before it has become cleaned. Then follows a period of 25-28 days during which the fly is incapable of producing infection. It is only when the parasites appear in the salivary glands that the insect becomes infective. The parasites in these glands resemble *T. gambiense* as seen in mammalian blood and they persist in the glands as long as the fly lives. Experiments made by inoculating the contents of flies into susceptible animals at various periods after an infective meal have given concordant results with those just mentioned. When the gut contents of a fly are injected into an animal within two days after it has been fed on trypanosome-containing blood, the animal becomes infected; from the third day onwards the results of similar inoculations are negative until about the 25th day, when injections of either the gut contents or salivary gland emulsion produce infection and these organs continue to be infective as long as the fly lives in captivity, *i. e.*, up to the 98th day or longer.[6] *Trypanosoma rhodesiense*, now recognized as distinct from *T. gambiense*, is more closely allied to *T. brucei* than to *T. gambiense*. It is conveyed by *G. morsitans* and occurs in Northeastern Rhodesia and Nyasaland in cases of sleeping sickness in man. Apart from morphological differences, it has been found to be more virulent than *T. gambiense* and to occur more plentifully in the blood of man and animals infected with the parasite. The high degree of virulence possessed by *T. rhodesiense* suggests that it is a new variety or species. Water-buck, hartebeest, impala, wart-hog and native dog have been found to serve as reservoirs in the sense previously described. Flies captured in a wild state or raised clean and then infected in the laboratory have been shown to transmit the trypanosome. The fly becomes infective in 11-15 days (Kinghorn and Yorke, 1912, in North Rhodesia) to 35 days (Taute, 1911, at Tanganyika) and, coincidentally with its becoming infective, the flagellates appear in the fly's salivary glands. Only about 5 per cent of captive flies fed upon trypanosomatous blood become infective, but, as in the case of *T. gambiense* and *G. palpalis*, the fly, once infected, remains infective as long as it lives and it does not "clean itself" of parasites after repeated feedings on trypanosome-free blood.

[5] It is worthy of note in this connection that Ross and Milne have shown that *T. rhodesiense* exhibits periodicity in respect to its numbers in the blood. Miss Muriel Robertson has just reported what appear to be negative periods in monkeys suffering from trypanosomiasis. Although trypanosomes can be found in their circulation, the flagellates do not appear to have reached a stage in their development when they are capable of infecting *Glossina*. She reports, moreover, that a greater proportion (up to 21%) of *G. palpalis* become infected if the flies are starved for several days after imbibing trypanosomatous blood.

[6] A *Glossina palpalis* ♀ has been observed to live 227 days in captivity. These flies live on an average 4½ months in captivity.

NAGANA.

Trypanosoma brucei is conveyed by *G. morsitans* and *G. palpalis*. The well-known disease, nagana, to which this trypanosome gives rise, has been repeatedly transmitted by means of *G. morsitans* captured in a wild state in Africa. The parasite possesses a wide range of pathogenicity and can be transmitted for an indefinite period from animal to animal by inoculation of blood. We still maintain a strain of *T. brucei* in Cambridge which came from Zululand 15 years ago in a dog suffering from nagana, and it has been maintained by passage from animal to animal apparently with undiminished virulence. The greatest sufferers from nagana are apparently horses and dogs, man being unaffected. Once infective, *G. morsitans* remains infective doubtless as long as it lives. Tested under experimental conditions, this fly has proved infective 88 days after first imbibing the trypanosome. Through experiments with flies bred in captivity and consequently "clean" to start with, it has been shown that *G. palpalis* may also transmit *T. brucei*. As in *T. gambiense* and *T. rhodesiense*, it has been found that this fly does not become infective until about the 18th day and remains infective up to the 66th day and no doubt considerably longer.

SOME OTHER GLOSSINA-TRANSMITTED TRYPANOSOME INFECTIONS.

Trypanosoma dimorphon and *T. pecaudi* also appear in the salivary glands when the flies become infective. These trypanosomes are transmitted by *G. tachinoides* and *G. longipalpis: T. dimorphon* may also be conveyed by *G. morsitans*.

T. cazalboui[7] is transmitted by several species of *Glossina* (*morsitans, palpalis, longipalpis* and *tachinoides*). When laboratory-bred flies are allowed to feed upon blood containing this trypanosome, 20-70 per cent of them become infected. *Glossina palpalis* becomes infective after 6-7 days[8] or after 17 days,[9] *morsitans* on the 9th day[8] or on the 21st-30th day.[8] After the fly feeds the parasites assume a crithidia-like form

[7] *T. vivax* is regarded as identical with *T. cazalboui*.

[8] According to French observers.

[9] According to British observers working in a different locality with "*T. vivax*."

(48 hours) and remain attached by the flagellar end to the labrum or hypopharynx; the infective forms, resembling trypanosomes, *remain confined to the region of the fly's proboscis.* Infection has been produced by inoculation of animals with the proboscides of infected flies. The flies presumably remain infective for life, *palpalis* conveying the trypanosome to susceptible animals 75 days after having infected itself.

In all of the species of trypanosomes which have been enumerated (*gambiense, rhodesiense, brucei, dimorphon, pecaudi* and *cazalboui*) we have no evidence that the parasites are transmitted to the offspring of the flies which serve as vectors. In all cases the trypanosomes may occasionally be transmitted mechanically by the fly for a brief period after it has imbibed infective blood, and this is followed by a more or less lengthy period during which the fly is uninfective. Then, coincident with the appearance of parasites resembling the blood forms of the trypanosomes in the salivary glands or proboscis (*T. cazalboui*), the flies become infective and remain infective indefinitely. There is evidence that certain of these trypanosomes favour definite species of *Glossina* as hosts; if it were not so the flagellates would be even more widely distributed geographically than they are at present.

FIG. 11.—*Conorhinus megistus* ♀ after chagas.

CHAGAS' DISEASE.

Schizotrypanum cruzi Chagas, 1909, the cause of trypanosomiasis in Brazil is transmitted by a reduviid bug, *Conorhinus megistus* (Fig. 11). This vector occurs all over Brazil in badly kept clay and wooden houses and is a night feeder, the adult insect being able to fly. The bug moults five times before attaining sexual maturity in about 324 days. The bug becomes infective eight days after feeding upon infected blood and remains infective over a year. A female may live over 57 days without food.

The parasites, which are numerous in the blood in acute cases, multiply in the midgut of the bug. They are at first rounded, then crithidia-like, they then assume the trypanosome form in which they occur in the gut and salivary glands of the bug. Infection occurs through the infected saliva of the bug introduced in the act of biting, but the bug's excreta are also infective when fresh. I may add that Brumpt has recently observed the development of *T. cruzi* in *Cimex lectularius* and *C. boueti.*

The disease is communicable to dogs, cats, rabbits, guinea-pigs, rats, mice, and monkeys (*Cercopithecus ruber, Hapale* and the Sajou). It is peculiar compared to other forms of trypanosomiasis, the thyroid gland being at times much enlarged (goitre-like). In some chronic cases there occur motor and cardiac disturbances, convulsions, infantilism and idiocy, etc.

TRYPANOSOMA BOYLEI LAFONT 1912.

Another interesting parasite of a reduviid bug, *Conorhinus rubrofasciatus,* has been reported upon this year by Lafont. The insect, which attacks man in Mauritius and Réunion, has been found to harbour flagellates, the intestinal tract of 50-80 per cent of the bugs containing the parasites. Lafont infected rats and mice by intraperitoneal injection with the gut contents of the bugs. In rats the parasites remain confined to the peritoneal cavity whence they disappear in about 30 hours. In mice, on the other hand, the flagellates appear in the blood stream in from 5-7 hours after inoculation and persist there for 1-5 days, after which they disappear and the mice usually die. When mice harbouring the trypanosomes in their blood, were bitten by the bugs, the flagellates resumed the forms (leptomonas, crithida and trypanosome) which they originally possessed prior to entering the body of the mouse.

THE RAT TRYPANOSOME (*T. lewisi*) AND ITS MODE OF TRANSMISSION.

Whereas in the *Glossina*-transmitted trypanosomes the parasites enter fresh hosts through the flies' proboscides, we have another method of infection in the case of the rat trypanosome.

Trypanosoma lewisi is conveyed by several species of flea and by the rat louse, it is world-wide in its distribution and occurs in 25-100 per cent of *Mus decumanus* captured in a wild state. Rats may harbour the parasite in sufficient numbers in their blood to render them demonstrable microscopically for a period lasting from a week to seven months. The usual vectors are unquestionably the common rat-fleas (*Ceratophyllus fasciatus* and *Ctenophthalmus agyrtes*) although the parasite is transmissible by other species of flea (*Ctenocephalus canis* and *Ctenopsylla musculi*) as has been demonstrated experimentally. Rat-lice (*Haematopinus spinulosus*) may occasionally serve as vectors.

Trypanosoma lewisi, after being imbibed by the flea, multiplies rapidly, chiefly in the hindgut and rectum of the insect. The parasites assume a crithidia-like appearance and occur in large bunches attached by their flagellar ends to the epithelium, or they occur in cyst-like masses within degenerating epithelial cells. Subsequently, the parasites resemble the blood forms as seen in the rat. They may then be found in vast numbers crowding the hindgut and rectum of the flea. The latter becomes infective in 4-7 days and it may remain infective for 45 days or longer. The flea does not infect the rat through its proboscis, and the parasites are not found in the flea's salivary glands. Infection can take place in three ways: the flea harbouring the infective forms of the flagellates may be (a) crushed and devoured by the rat, (b) the rat may lick

its fur upon which an infected flea has just dejected, (c) the rat may lick and infect with flea dejecta the wound produced by the insect. Fleas in the act of feeding frequently eject excreta which may be loaded with the flagellates in the infective stage. We have conclusive experimental evidence to prove that infection may occur in these different ways. We have then, in the flea, an entirely different mode of trypanosome transmission as compared to what we have seen in *Glossina*.

LEECH-TRANSMITTED TRYPANOSOMES OF FISH, REPTILIA AND AMPHIBIA.

Trypanosoma granulosum, occurring in the eel, develops in a leech, *Hemiclepsis marginata*. The flagellates at first multiply actively in the leech's stomach and afterwards in the intestine, where crithidial forms occur. Finally, the flagellates reassume the trypanosome form and appear in the proboscis-sheath of the leech. The latter only becomes infective when the flagellates appear in this situation.

The Trypanosomes of the gold-fish, bream, perch and rudd

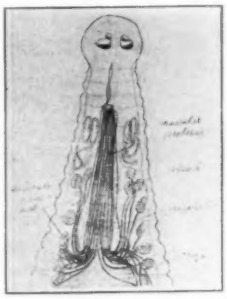


FIG. 12.—*Hemiclepsis marginata*, anterior portion of living leech, showing position of trypanosomes or trypanophasms in the proboscis sheath. After Robertson.

all develop in *Hemiclepsis marginata* (Fig. 12). They multiply enormously in the crop, undergoing a great change in appearance, being tadpole-like in form and having a crithidia-like arrangement of the nuclei. After the eighth day, slender trypanosomes appear, and after the tenth day they gather progressively in the leech's proboscis-sheath, where they cease to divide. The leech's bite is now infective and the flagellates are cleaned out of the sheath during the process of biting. The times when the leech becomes infective depends entirely upon the rate of the leech's digestive processes, it may be delayed to the 35th day, or longer. The leech still continues to harbour the trypanosomes; others present in the gut succeed those that disappear from the proboscis after each feed.

This leech may produce a mixed infection in fish for it also transmits *Trypanoplasma cyprini* which occurs in gold-fish and tench. This parasite divides rapidly in the crop, slender forms appearing on the second day and advancing on the sixth day so as to accumulate in the leech's proboscis-sheath in vast numbers. The flagellates attach themselves in this situation by their flagella and tend to crowd forward as the leech's digestion approaches completion, with the result that the leech may completely clean itself of parasites at a single feed. It is worthy of note that the trypanoplasm does not materially alter its morphology in the leech. (Robertson.)

Trypanoplasms have also been transmitted by the leech, *Piscicola geometra*, and a number of trypanosomes occurring in fresh and salt water fish (*T. danielewskyi, T. soleae, T. rajae, T. cotti*) have been transmitted experimentally by different species of leeches (*Hemiclepsis, Pontobdella*, etc.).

Trypanosoma inopinatum, which occurs in the green frog, is similarly conveyed by a leech. In this case, according to Brumpt, the flagellates are transmitted hereditarily to young leeches, thus offering a marked exception to what takes place in all other trypanosomes whose vectors have been determined. The leech concerned is *Helobdella algira*, and by means of this vector the trypanosomes have been successfully conveyed to *Rana esculenta* in which the flagellate does not occur in nature.

Finally, I would mention *T. vittatae* which is parasitic in a tortoise (*Emyda vittatae*) in Ceylon. Thus flagellate is transmitted by a leech (*Glossosiphonia*) in which it appears to behave in a similar manner to the fish trypanosomes above enumerated.

The general trend of recent work has gone to prove that, in the majority of instances, the trypanosomes of vertebrates are transmitted by blood-sucking ectoparasites within which they undergo a cyclical development. Whereas in the case of the *Glossina* mechanical transmission may occur, it must play a subsidiary part. In *Glossina, Conorhinus* and leeches, infection occurs through the mouthparts of the vector; in most Glossinas the flagellates are expelled from the salivary glands. In but a single instance (*T. inopinatum*) has it been claimed that the offspring of the vector (a leech) becomes hereditarily infected, and the statement awaits confirmation. In the rat-trypanosome there occurs a contaminative infection through the dejecta of the fleas or lice which attack a fresh host. Fleas and lice do not become hereditarily infected with *T. lewisi*. In dourine (*T. equiperdum*) direct infection from host to host in the act of coitus appears to be the rule, whereas it may occur exceptionally in other trypanosome infections. We are still ignorant as to the usual mode of infection in many trypanosomiases, including surra and mal de caderas. In both cases the parasites (*T. evansi* and *T. equinum*) possess a wide range of pathogenicity and may produce chronic cases, so that there is every reason to believe, in my opinion, that reservoirs may play an important part in maintaining these diseases in nature.

POWERS OF ADAPTATION SHOWN BY TRYPANOSOMES.

Investigations conducted during the last few years have shown that trypanosomes possess considerable power of adaptation to altered conditions in the host, such as may be brought about by the administration of drugs. Trypanosomes may acquire a great resistance to the effect of a drug. At times this acquired resistance is accompanied by changes in their morphology, at other times no such changes occur. In the case of *T. brucei*, which becomes resistant to pyronin and

oxazine preparations, the acquired drug-resistance is accompanied by the disappearance of the blepharoplast. If these drugs are administered to an animal harbouring the trypanosome in its blood it will be seen that 40-90 per cent of the trypanosomes no longer show blepharoplasts after the expiration of 24 hours from the time the drug was administered. In this respect the oxazine preparation is the more powerful drug. If such trypanosomes are now passed through a series of 10 rats, each rat being in turn treated with the drug, it will be seen that the trypanosomes acquire a great resistance to the drug and that, with time, they no longer show blepharoplasts. If the trypanosomes have been subjected to the continuous effect of the drug for longer periods the blepharoplasts will not be reacquired even when the trypanosomes are passed through a series of 130 untreated animals. The oxazine preparation acts directly upon the blepharoplast. In trypanosomes which have reacquired their blepharoplasts a change of constitution has been brought about, for when they are subjected to the effects of arsenicals or tryparosan they again lose their blepharoplasts, this being contrary to what is observed in the normal flagellates.

In other cases no appreciable alteration in morphology accompanies the acquisition of drug-resistance. *Trypanosoma brucei* has been rendered resistant to parafuchsin (Francke and Roehl) and to atoxyl (Browning). In the latter case, this trypanosome has been found to remain drug-resistant during its passage through 140 untreated animals, this representing many generations of trypanosomes. There are, however, limitations to this resistance. Thus, Mesnil and Brimont found that *T. evansi,* rendered resistant to atoxyl to such a degree that the strain still remained resistant after passing through 110 untreated mice, when transferred *to another host,* the rat, immediately became susceptible to the drug whilst the rat served as its host. When the flagellate had passed through a series of 10 rats it was found, however, to be still atoxyl-resistant when returned to the body of the mouse. Similarly, atoxyl-resistant *T. equiperdum,* rendered resistant in the body of the donkey, has been passed successively through rats, guinea-pigs, rabbits and rats during a period of seven months and been found atoxyl-resistant upon being returned to the animal, the donkey, in which it was originally rendered resistant. From this we may conclude that atoxyl combines with a blood constituent to act upon the trypanosomes. When the flagellates have acquired resistance to atoxyl+mouse blood, they are still susceptible to atoxyl+rat blood or other blood than that of the mouse.

Of considerable interest, moreover, are certain observations of Gonder's (1911) upon arsenophenylglycin-resistant *T. lewisi,* wherein it was found that the resistance was retained for upwards of three months in cultures, but *lost* after a sojourn in the rat louse by which, as we have seen, the parasite is transmitted. The drug resistance is lost by the flagellate after about 10-12 days in the louse, and this fact may be brought forward in support of the view that the louse is a definitive host of the trypanosome and that a sexual development of the parasite occurs in the louse—the sexual process, at a stroke, eliminating acquired characters previously maintained for thousands of asexual generations during the passage by inoculation from rat to rat.

This observation has a practical bearing in respect to human trypanosomiasis where arsenic-resisting strains of *T. gambiense* would be assumed, under certain conditions, as likely to be transmitted by *Glossina.* It will doubtless be found in this case, as with *T. lewisi,* that the passage of the flagellate through its vector renders it again susceptible to the action of trypanocidal substances.

In the time at my disposal I have only been able to dwell upon certain aspects of the subject of trypanosomiasis, and to bring out some of the many interesting problems which are being gradually solved by many workers.

The preventive measures directed against sleeping sickness have been dictated by experience gathered from research into the etiology of the disease, and, as our knowledge advances, so will our measures for combating the scourge have to be modified.

The hope that the disease would be exterminated by resorting to the inspection and segregation of natives, to depopulation and the destruction of the habitats which are suitable breeding grounds of *Glossina palpalis* have been but partially realized. The prolonged period of incubation and chronicity of the disease, coupled with the fact that fatal relapses have been known to occur after the lapse of years in apparently recovered cases render the disease very difficult to combat. A measure of immunity appears to be acquired after recovery, judged from animal experiment. Although treatment has given results which are encouraging, we are still far from the goal we wish to attain. The question of reservoirs has grown to be one of the greatest practical importance and the cry for the destruction of the game animals which serve as such is growing louder. It is for this reason that game destruction is at present being carried out over limited areas to see if it exerts any beneficial effect, although it appears very doubtful that this measure will prove useful, since it will drive the game elsewhere and so scatter the reservoirs into other regions. It is, moreover, by no means certain that domesticated animals would not have to be likewise destroyed, for they, too, may act as reservoirs. In view of the wide range of pathogenicity possessed by *T. gambiense* there is always the possibility of animals serving as reservoirs which it will be practically impossible to exterminate. On the other hand, there is hope that by reducing the number of reservoirs and *Glossinas* that the chain of parasitism may be broken, as it may be in malaria by mosquito reduction. Judging from the observations on *Glossinas* captured in a wild state, but a very small number of these are infective; the percentage of such flies may be sufficiently reduced to greatly lessen the danger of infection through their agency. In the case of *G. palpalis,* which has a relatively stationary habitat in proximity to water, we have a comparatively easy problem to deal with as compared to *G. morsitans.* The latter fly, which conveys *T. rhodesiense,* is migratory, it ranges widely and it resists dry-

ness such as *G. palpalis* cannot withstand, and, therefore, to attack its habitats successfully is practically impossible. A measure of protection will no doubt be afforded by putting the land, in the vicinity of human habitations, under suitable cultivation. We know that the main roads of travel are the most dangerous and that the old native measure in respect to nagana of avoiding the fly belts during the day is safely to be relied upon.

It is clear that the study of the biology of the carriers of trypanosomes has become one of great practical importance, and that we are gradually accumulating data upon which we can proceed in a rational manner to combat trypanosomiasis.

NOTE.—Those desiring to consult the literature of *trypanosomiasis* are referred to the *Sleeping Sickness Bulletin*. The lecturer has purposely refrained from giving references so as not to burden the text.

THE CHILDREN'S HOSPITAL, THE MEDICAL SCHOOL AND THE PUBLIC.*

By L. EMMETT HOLT, M. D., New York.

The opening of any new hospital is an event which it is fitting we should celebrate, and I deeply appreciate the honor of being invited to a personal participation in the opening of the Harriet Lane Home for Invalid Children. A new hospital for children in this city means much to the community and to the medical school. I congratulate the City of Baltimore and The Johns Hopkins Medical School upon this event, and upon the selection which has been made of the head of this new institution, one of whom I can speak from most intimate personal and professional relations which have extended over a period of more than twelve years. I congratulate Dr. Howland on the opportunities which this splendid new hospital offers for teaching, for research and for practical experience. This building completed, and now formally opened, is the realization of the idea of a hospital for children in Baltimore which began to take shape when Dr. Emerson made his instructive report to the university upon children's hospitals in this country and abroad. If events have moved slowly they have moved surely.

We have in this country been slow to appreciate the need of special hospitals for children. Just as the specialty of pediatrics has been gradually differentiated from obstetrics on the one hand and general medicine on the other, so the evolution of the special hospital has been a slow one. Homes for foundlings most of our large cities have provided for many years. These, though necessary, have been in no sense hospitals; and often lacking in proper medical control, by their excessive mortality they have served as an example of how little philanthropy without science can accomplish in saving infant life.

In maternity hospitals infants are tolerated as one of the unavoidable incidents of obstetric practice. But the provision for them, and the attention bestowed upon them, even in our best institutions, is something which shocks the pediatrist. Certainly they have as yet failed to appreciate the hospital requirements of young infants.

The need for special hospitals for contagious diseases is latterly becoming generally felt. Of the fifty cities in the United States with a population over 100,000, thirty-four have already established hospitals for the reception of the common contagious diseases, scarlet fever, diphtheria, etc. All but ten of these have come into existence since 1900. They are most important but limited in their sphere of activity. They have not supplied the need of a place where the common diseases of infancy and childhood can be studied and treated.

The necessity for special hospitals entirely devoted to children is something which is even yet scarcely appreciated in the United States either by the medical schools or the public. Only twenty-two cities are now provided with special hospitals for children. Is there a need for such institutions? Since hospitals are for the care of the sick, one may well inquire, who are the sick? Vital statistics of New York City show that twenty years ago 41 per cent of the total deaths were in children under five years, and that now, in spite of the great reduction which has taken place, these still form 33 per cent of all deaths. In the United States Census for 1910, Baltimore ranks seventh among the cities having the highest infant mortality, being exceeded only by Fall River, Lowell, Richmond, Detroit, Pittsburgh and Scranton. New York, with all its overcrowding, ranks fifteenth. The mortality in Baltimore of children under five years is the ninth largest in the cities of the country having a population over 100,000. It is surely incumbent upon the public to see to it that the age which includes fully one-third of all deaths should have adequate hospital provision made for it, and, what is even more important, adequate facilities given to specialists for study and investigation, and at the same time afford to students, practitioners and nurses opportunities for instruction and experience.

It is often urged that wards for infants and children in general hospitals are to be preferred to separate hospitals for this group of patients. Such wards have, it is true, been a part of the organization of the larger hospitals of most of our cities for the past fifteen or twenty years. But how has this worked? In many institutions the beds have been largely or exclusively given over to the care of orthopedic or other surgical cases. Where medical beds existed they have usually been made a part of the general medical service of the hospital, and the attending physicians who served in rotation a few months at a time, as a rule, gave scant attention to the needs of the special service. Equally unsatisfactory has been the attention given by the resident medical staff, when each

* Address delivered Nov. 20, 1912, at the opening of the Harriet Lane Home for Invalid Children, The Johns Hopkins University.

member was given in turn two or three months in charge of this ward that he might gain some experience with children. The practical result of such an organization and administration has been that the service, especially as regards the infants, went by default, and very little was accomplished in advancing the knowledge of the diseases of children. With respect to organization there has been in some places an improvement by the appointment of a special attending physician to these wards. This is a practice which should invariably be followed. Yet in spite of this change I have personally no hesitation in pronouncing in favor of the separate hospital. The children's service in the general hospitals is in nearly all cases too small to admit of a proper classification and separation of patients. The only important argument which I think can be advanced in favor of wards in general hospitals is that of economy. A large institution can certainly be operated at a lower *per capita* cost than a small one, and the children's hospital must not be too large. That such a service as usually operated affords a valuable experience to the resident medical staff is open to serious question.

The construction, the equipment, the organization, and the operation of a hospital for young children are quite different from those needed in hospitals for adults. These grow out of two great difficulties which attend the hospital care of these patients: the problem of nutrition and that of ward infections. These necessitate smaller wards, ampler provision for the separation of patients in doubtful diseases, and in diseases of feebler communicability than our ordinary contagious diseases. Not only must there be sufficient provision for fresh air and proper ventilation for acute infectious cases and pneumonia, we must have also wards in which a temperature much higher than the usual room temperature can be maintained for the congenitally feeble, the marantic and the premature infant. The nutrition of feeble infants is always difficult even in a state of comparative health; but with acute illness added, the difficulties are greatly increased. The feeding especially must be exact and requires special equipment and specially trained service. There are many other particulars in which the operation of an institution caring for the very young must be carried on in an entirely different manner from methods pursued in an adult hospital. It has been my observation and experience that boards of managers, hospital superintendents, and head nurses can rarely be made to appreciate them. Forming only one department of a large institution, and that usually a small part, it is seldom the case that anything like adequate attention from an administrative point of view is given to the wards for infants and young children.

In the past our hospitals have represented our philanthropy. The modern hospital, while not losing its philanthropic character, is to be classed among the institutions of higher education. The academic hospital in particular is to be so regarded. Properly equipped and administered, it is altogether the most productive of all the college laboratories. Proper teaching does not interfere with the best care of the sick, but rather should contribute to it. This is particularly true of little children, who have no prejudices to overcome, no modesty to be shocked, and no sensibilities to be hurt; but since they cannot describe their pains or express in words their wants, they require the closest kind of individual study and observation. No better opportunity can be afforded for the training of the medical student than to place him in a hospital ward with sick infants and teach him how to observe them. One who would succeed in this specialty must not only know disease, he must learn to understand children.

The provision for the care of patients must be of the very best; while not extravagant the best possible hygienic conditions for the treatment of the sick must be furnished. While it is important to give our students the scientific point of view, we must, at the same time, equip them with the facts and the training which will enable them to do as well as possible the common everyday things which are needed in practice. It is altogether probable that fully four-fifths of your students will be practitioners of medicine, and that the other fifth will, as parents, be called upon to put to practical use the teaching of this department.

Research work, while of the utmost value to the hospital, is of little importance to the average student. Now and then a genius appears in our medical schools who should be encouraged to take up new problems. But there are few men who are not the better for having spent four years, as a preliminary training, upon the regular courses. Only in this way can they obtain the breadth of view which will enable them to connect their scientific work with the great practical problems of medicine to-day.

Provision for research in the special hospital should be ample, and this department should be generously supported, for here are opportunities found in no other institution. The close association of the scientific and the practical workers under one roof is of immense advantage to both. Research work should not be conducted along pathological or chemical lines only, but it should be clinical also. All these lines of investigation should be carried on simultaneously. The present disposition to undervalue the clinical side and put the emphasis upon the purely laboratory side of research is most unfortunate. Students and young assistants should not get the idea that the only scientific observations in medicine are those made on guinea pigs. There is urgent need at the present time not only for technical training in the use of the newer aids to diagnosis, but for the closest kind of clinical observation of disease, especially in young children. Nearly the whole fabric of infantile therapeutics must be constructed anew from the standpoint of recent advances in medical science.

I do not mean that patients in the hospital are to be used as subjects for experiment; that phrase is likely to be misunderstood. But what is new and promising must be thoroughly tested under conditions in which the most careful observations are possible; and these can only be obtained in a hospital. Proper clinical studies upon patients necessitate a liberal provision for a resident staff and assistants. Their work, however, can, as already suggested, be advantageously supplemented by the medical student. All these three lines of work, student instruction, research, and the care of patients can be

carried on at the same time and each activity, instead of embarrassing the others, can promote them and thus the best possible results in all be attained.

I have already suggested that hospital work among very young children is quite a different problem from the hospital care of adults. There are some features upon which I would like to dwell for a few minutes. The first is that of hospital mortality. Nothing is more disturbing to hospital managers, nor at times more discouraging to a medical staff than the death rate, especially among infants. While, in a broad sense, it is true that the value of the work is to be measured by the number whose lives are saved or whose health is restored, this must not be too narrowly construed. To compare the mortality figures of such a hospital with one admitting only adults is most unjust. The proper comparison is between young children treated in a hospital and those of the same class treated outside of it. We have seen that children under five years furnish a third of all the deaths. In different cities the mortality during the first year of life varies from 150 to 350 per 1000 of infants born. Infants are the first to feel the effects of an unfavorable environment, they are the most susceptible to disease and have the smallest resistance to it. Whether they are received into hospitals or not the mortality of infants is very high, unnecessarily high. In the City of Baltimore your infant mortality in 1910 was 383 per 100,000 of population.

It is to reduce this excessive death-rate to the minimum that the hospital for children must work. Obviously any such institution which does its duty to the community, and admits very sick infants, will have of necessity a high death rate. This can, of course, be reduced by the simple expedient of refusing admission to apparently hopeless cases. I have known institutions which resorted to this in order to make a good showing in annual reports. But it is a narrow and contemptible sort of philanthropy which would countenance such a practice. A hospital exists for the sick, and the sicker the patient the greater the reason why he should be received in a hospital which is presumably equipped with every facility for saving life. Nearly one-fifth of the deaths in the Babies' Hospital, in New York, are in patients who live less than twenty-four hours after admission. But if such children were not received, in many instances, they would have died in the mother's arms while walking the street. For a period of years in this institution, which receives only infants and children under three years, the average mortality has been about 30 per cent. Something like this is to be expected in every hospital which admits the same class of patients. But to hospital managers I would say, do not measure the usefulness of your institution to the community by the death rate, but regard this as an indication of the kind of patients admitted. Year by year as science advances, and your institution grows in efficiency, you will note with satisfaction a steady reduction in the death rate with the same class of patients.

Another feature of hospital work among very young children is the frequency of ward infections. Not only are measles, scarlet fever, whooping cough and diphtheria to be guarded against, but more difficult to combat because the means of spreading is less obvious are infections due to the pneumococcus, streptococcus, gonococcus, and influenza bacillus. They are responsible for many more deaths than are the common contagious diseases. All of these necessitate the detention of patients in observation rooms before admission to the general ward; adequate space between cribs, or the erection of partial partitions between them to prevent bed to bed infection, hygienic sweeping and dusting; the most scrupulous cleanliness in wards to prevent aerial infection through dust; constant care regarding towels, bath tubs, wash clothes, napkins, thermometers, and in fact everything which comes in contact with the patient. All of these things and many more which time does not permit me even to enumerate, indicate that in a hospital ward for infants we must aim at conditions which at present, in most institutions, are realized only in the surgical operating room. The susceptibility of these patients to infection is certainly comparable to persons with open wounds. You are thinking, perhaps, that what I have said is impractical or impossible, and that it would not be worth while. So surgeons once thought of rigid asepsis. Hospital work for infants is admittedly difficult. Unless it can be well done it should not be attempted; but when it is properly done, the results will bear comparison with those obtained in any other department of medicine.

I have not time to dwell upon the necessity for the most ample provision for nurses, if such results as we have been contemplating are to be obtained. The needs of adult patients in this respect are no criterion. At least one nurse to three infants by day, and one to eight or nine at night are necessary even for patients not acutely ill.

The conditions under which only successful hospital work for young children can be carried on impose certain limitations with regard to the size of such an institution. I do not believe that the best work is possible in hospitals of this class with three or four hundred beds. Several small ones would accomplish much more. The one hundred beds provided in this institution I do not think should be increased. This will provide probably an average number of seventy-five patients, which will furnish ample material for the instruction of students, and are all that can advantageously be cared for by a single medical head. This ward service should be supplemented by an out-patient department which may be of indefinite size.

On the part of hospital trustees and managers there is often a disposition to consider the size of the work done as a measure of usefulness. But it is the quality of the work by which a hospital should be judged, not the quantity, for if the quality be poor, the larger it is the worse for the public and the profession. Numbers do not count in science so much as other considerations.

In New York, at least, the greatest embarrassment to the scientific study of disease in hospitals is the size of the service, and the demands made upon the medical and nursing staff for the routine care of the sick. The time needed for the thorough study of difficult and obscure cases is not to be found and progress in clinical medicine is therefore slow. I mention these points, not because they are new, for every hospital

physician fully appreciates their force, but in order that lay members of hospital boards may get the point of view that the chief function of a children's hospital is to determine, by careful observation in the diagnosis and treatment of the few, how the many must be treated. The best results are to be obtained by the intensive method of study, not the statistical method.

Some of the discouraging features of hospital work for children have been mentioned. There is another side of greatest encouragement. The great difficulties are to be found in the first year. After this age children are the most hopeful patients to deal with. Nowhere else does effort tell so effectively in results. With adults hospital work is, much of it at least, only patchwork, putting an old hulk into such repair that it may keep afloat and do duty a little longer. With children it is more like new construction, starting a new life straight, with all the satisfaction which this brings.

A special hospital like this can do much for the community besides caring for the sick poor. It sets a standard of medical practice for the profession of the city. It is an exponent of modern science in its particular field. Here should the best hygiene be illustrated, the best feeding be practiced, and the most intelligent care of the infant sick or well be exemplified. Such ideas spread gradually from those immediately connected with the hospital to the general public.

One of the most effective means of influencing the public is by nurses who have been educated in the institution. Not only should trained nurses be taught a knowledge of children and their diseases, but a school for training nursery maids in the care of healthy infants should be established as a constituent part of the hospital. The need of the public in this respect is so great that the opportunities which the hospital affords to give this instruction should be utilized. This is a by-product of hospital organization and operation that is of great importance, and will prove of advantage to an institution needing public support.

The educational value to the public of an up-to-date special hospital like this can hardly be exaggerated. It is destined to take its place among the great forces for social uplift in the department of child welfare. The City of Baltimore should have as much interest in its development and as much pride in its success as the medical school. The people of the community will need to be educated up to the advantages which the hospital offers over the home, especially the homes of the poor, for very sick children. With many of this class a prejudice against the hospitals, born of ignorance, must be overcome before they will consent to entrust their children to its care. To gain confidence is a matter which takes time, but the establishing with parents and relatives the most friendly and sympathetic relations is something, the importance of which every one connected with the hospital as superintendent, doctor, nurse, or employee should appreciate. It has to do with the practical success of the institution in many ways. Upon no one thing does the accurate diagnosis of disease depend so much as upon autopsies. The facilities which the hospital affords for seeing autopsies constitute one of its greatest uses. I know of children's hospitals where these are permitted upon less than 10 per cent of the fatal cases. What a loss to science this represents. For the medical staff and students who have long watched an obscure condition go on to a fatal termination, not to have an opportunity to clear up the mystery is most discouraging. In another institution with which I am personally connected, consent for autopsy is obtained in 70 per cent of the cases; and this has been accomplished largely through the influences which I have just suggested.

The hospital occupies a place in modern civilization of steadily increasing influence and importance. On the one side it must be in close touch with teaching and medical research, and on the other with the needs of the public. The spirit of an institution is something different from its aims. It is the resultant of the attitude of mind, the breadth of outlook, and the personality of the three persons who determine the hospital's policy: The dominating spirit in the board of trustees, the superintendent, and the physician-in-chief. A hospital should be managed efficiently and scientifically, but more than this, it should be managed humanly, keeping in sympathetic relations with the class who form its patients. May we in this country, be delivered from the cold-blooded science which dominates so many of the hospitals abroad, where patients are regarded only as so much *material*. We must not forget in our hospitals, or in our medical teaching that the ultimate aim in all our work is to minister to the suffering and the unfortunate. We need to keep such ideals before the minds of the medical student quite as much as to arouse his enthusiasm for science, and to arm him with the skill and experience which will fit him to practice his profession.

IN MEMORIAM.

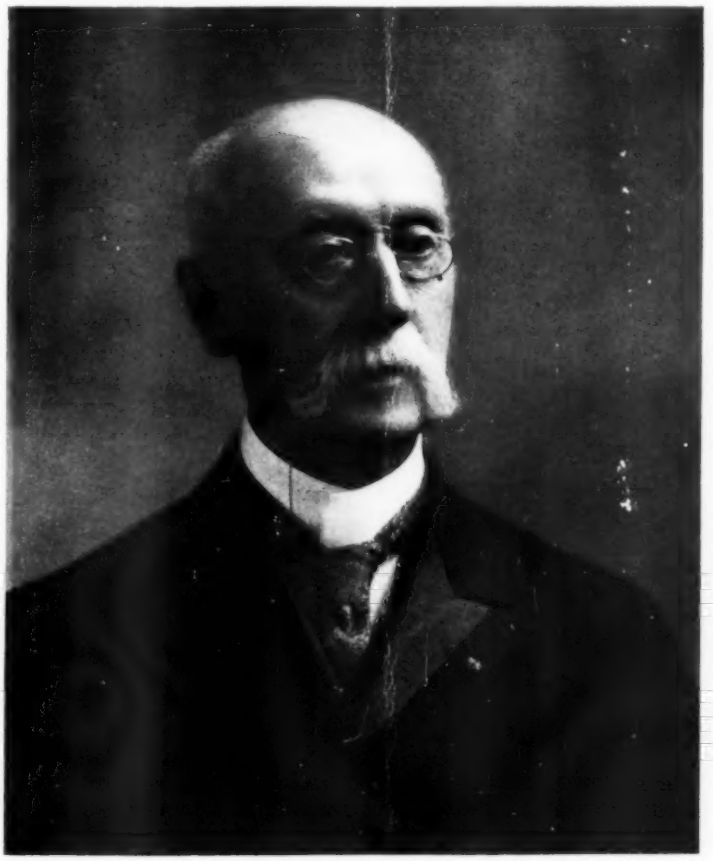
DR. ROBERT FLETCHER.

Doctor Robert Fletcher, for thirty-five years the principal assistant librarian of the Library of the Surgeon General's Office, died in Washington, November 6, 1912, in the ninetieth year of his age. The end of such a long and useful life calls for more than passing notice, for to the great learning and accurate editorial work of Dr. Fletcher on the Index Catalogue and Index Medicus the medical profession of America and Europe is deeply indebted.

Doctor Fletcher was born in Bristol, England, March 6, 1823, the son of an attorney and accountant of that city. He was educated at private schools in Bristol and read law with his father for two years before taking up the study of medicine at the Bristol Medical College and later at the London Hospital, of which he was the oldest living graduate. He became Licentiate of the Society of Apothecaries and member of the Royal College of Surgeons in 1844, married in 1843 Miss

Hannah Howe of Bristol, and came to the United States in 1847, making his home in Cincinnati.

At the outbreak of the Civil War Dr. Fletcher was commissioned as Surgeon in the 1st Ohio Infantry and was on active field service for two years. In 1863 he was made Surgeon U. S. Volunteers and assigned to the army of General George H. Thomas in the Nashville campaign. He was in charge of Hospital No. 7, Nashville, Tennessee, and subsequently medical purveyor at Nashville and Cincinnati where he wound up successfully the complicated affairs of a war-time purveying depot, receiving for "faithful and meritorious service during the War" the brevets of Lieutenant Colonel and Colonel. The War Department employed him in 1871 to assist in the preparation of the two valuable volumes of "Medical and Anthropological Statistics" of the Provost Marshal General's Bureau, derived from the examination for military service of over a million men. For this work Dr. Fletcher wrote the introductory treatise on anthropometry, about the only thing of interest to the general reader in this book, and which illustrates very well the extent of his information and his love for the historic and artistic aspects of medical science.



ROBERT FLETCHER.

The library of the Surgeon General's Office, an absurdly small and insignificant collection of books in 1861, had increased during the war to about 1700 volumes. In 1865 Dr. John S. Billings, then Assistant Surgeon, U. S. Army, was put in charge and began to develop what is now perhaps the largest and best known medical library in the world, a monument to the energy and forethought of its founder. As the library rapidly increased in size and importance, Dr. Billings prepared the plan of the present Index Catalogue in which under a single alphabet and in dictionary order a combined index of authors and subjects appears. The "specimen fasciculus" of the proposed catalogue was printed in 1876 and submitted to libraries and bibliographers for comment and suggestions. Soon after its appearance the services of Dr. Fletcher were secured as principal assistant to Dr. Billings in the work of preparing and printing the Index Catalogue of which the first volume was published in 1880. From that time to the past year (1912) a volume has appeared annually, and the first series A to Z having been completed in 1895, the second series now reaches the letter T. On these 33 massive quartos averaging nearly 900 pages to a volume and containing to date 327,000 author titles and 1,333,079 subject titles of books, pamphlets and original papers in periodicals, Dr. Fletcher labored to within a few weeks of his death, supervising, proof reading, and correcting with tireless patience and extraordinary accuracy. Much original work of a high order is called for in the grouping and subdivision of the subject matter of the Index Catalogue, requiring a vast amount of information which must be kept abreast of the times by constant study. The almost revolutionary changes in medicine and surgery and the evolution of many specialties which characterized the last years of the nineteenth century and the beginning of the twentieth, found Dr. Fletcher already an old man, but to the last he constantly added to his great store of knowledge and his fine intellect as readily appreciated the latest medical paper of real value as the venerable volumes of the old masters of medicine in which his bibliophile's heart delighted.

The Index Medicus, a monthly publication based upon the card catalogue of the Library of the Surgeon General's Office, and which supplements the Index Catalogue by bringing to the public notice the current medical literature before it can be reached in alphabetical order, was begun in 1879 with Dr. Billings and Dr. Fletcher as co-editors and ran until 1899 when the publication ceased. It was revived in 1903 under the auspices of the Carnegie Institution with Dr. Fletcher as editor-in-chief until his resignation in the early part of 1912.

Away from his editorial work Dr. Fletcher found time for many social and literary interests. He was sometime president of the Anthropological, the Philosophical and the Literary Society of Washington and the president of the Cosmos Club. He lectured on medical jurisprudence at the Columbia University of Washington, 1884-1888, and at the Johns Hop-

kins University, 1897-1903. In spite of, or perhaps on account of, his tireless editorial research he was led to pursue some of the side paths in medicine of special interest to him, and as a result he produced many original essays on anthropology, early jurisprudence and medical lore, as known to the old poets, dramatists and artists. In his writings, he is always master of his subject, clear and simple in style and with a certain quiet humor which is most attractive.

A complete list of his literary productions will soon appear in the Index Medicus, the last essay "On Some Diseases Bearing the Names of Saints" having been published after his death in the December number of the Bristol Medico-Chirurgical Journal preceded by a graceful "In Memoriam" by Sir William Osler, a friend of many years standing.

Doctor Fletcher was a handsome soldierly man, dignified and courtly in manner. He also possessed to the full the blessed sense of humor and was a philosopher who had learned to extract all that is best in life. Time dealt very gently with him. Except for the feebleness of extreme old age his health was excellent and his mind remained unimpaired.

Dr. Fletcher's service to the profession was acknowledged by many honors, among which was a banquet given by leading physicians and scientists on January 11, 1906, with a loving cup and a commemoratory album which was one of his most prized possessions. In 1910 he was awarded the gold medal of the Royal College of Surgeons, a rarely conferred distinction. He was an associate fellow of the College of Physicians of Philadelphia, honorary M. D. of Columbian University and a few weeks before his death received a degree in medicine from his first medical school in Bristol. He had many devoted friends, young men as well as old, who delighted in his company and enjoyed his conversation at his favorite club or in his charming private library where he lived alone with his books.

W. D. McCaw, M. D.,
Lt.-Col. (M. C.), U. S. A.
Librarian Surgeon-General's Office.

NOTES ON NEW BOOKS.

Bacteria in Relation to Plant Diseases. By Erwin F. Smith. In charge of the Laboratory of Plant Pathology, Bureau of Animal Industry, U. S. Department of Agriculture. (*Published by the Carnegie Institution of Washington, 1912.*)

The second volume of Dr. Erwin F. Smith's Bacteria in Relation to Plant Diseases, which bids fair to become the most exhaustive and authoritative work on the subject of plant bacteriology in the English language has recently appeared. The first volume was published in 1905. To understand the significance of these two volumes it is necessary to remember that it was the botanists of the old world who laid the foundations upon which the modern science of bacteriology was built up. The fundamental investigations of Ferdinand Cohn in the Botanical Institut of the University of Breslau paved the way for the epoch-making discoveries of Robert Koch in the domain of the bacteria pathogenic for animals and man. To the botanist of the decades from 1870 to 1890, however, bacteria were objects of study because of their biological or botanical characters. They formed an important part of those natural objects which came directly within the sphere of botanical investigation. The fact that bacteria themselves, classed among the lowest forms of plant life, could be the cause of important diseases of plants seems to have been recognized but slowly by the botanist. Indeed, as Dr. Smith points out in the historical introduction to Volume II, up to the year 1893 but a small number of plant pathologists were interested in trying to determine whether the bacteria, which were becoming recognized the world over as standing in etiological relation to the diseases of man and animals could also stand in analogous relation to those of plants. Of these earlier investigators Dr. Smith mentions as most important Burrill, Prillieux, Wakker and Comes, names relatively unfamiliar to the average student of bacteriology, who has limited his reading to that side of the subject presented in our text-books. It is interesting to note that the first of these, Burrill is an American, Professor of Botany in the University of Illinois, and that he established the bacterial origin of a disease known as pear blight, according to Dr. Smith, by investigations in the five years from 1878 to 1883. Of the others given special notice by the author, Prillieux, who proved that a disease of the wheat kernel was due to the growth of bacteria, is of French nationality. Wakker, who worked on a yellow disease of hyacinths, was a Hollander and Comes who recognized "bacteria in the tissues of diseased plants as early as 1880," an Italian. Despite this early work plant bacteriology as a well ordered science, apparently lagged far behind its sister science, animal bacteriology, and even as late as the latter part of the decade from 1890 to 1900 there seems to have been a serious doubt in the minds of certain plant pathologists as to the exact relation of bacteria to plant diseases. The last few years have seen, however, a rapid and fruitful development of the subject until at the present time it must be recognized as of a magnitude and importance equal to that of animal bacteriology. In 1893 Dr. Smith began a careful systematic study of the bacterial diseases of plants in his laboratory in Washington and the two volumes thus far published may be said to represent some of the results of this work, although many of his experiments and conclusions have already been presented in contributions to various journals and society meetings. The first volume appeared in 1905. It is devoted to an exhaustive analysis of the literature, to detailed description of methods and technique, to accurate formulas for stains and media. In a word, it is essenially an elaborate introduction to the science of bacteriology and as such is extremely useful to workers in any of its branches. But a few diseases of plants are considered in this volume and these only to serve as illustrations for the general subject matter. Particular attention is paid to the discussion of classification, that of Migula being adopted. The treatment of such topics as nomenclature, morphological and cultural characters in relation to species identification is far more elaborate than obtains usually in our text-books. This of itself is of great value, especially to the student of the bacteria pathogenic for man and animals, whose chief interest has centered so long in determining the effects of microorganisms upon the animal tissues and who is apt to overlook the wide and interesting side of the subject represented by the botanist. Finally the bibliography in Volume I is most elaborate. It covers 63 pages and is arranged according to subject, but in chronological order. As arranged it is capable of serving as a constant source of information in general bacteriology. In Volume II Dr. Smith continues his subject by further notes on the historical development of plant bacteriology and by general considerations on the relationship of bacteria to

plant diseases. Such topics as the mode of infection of plants by bacteria are considered exhaustively and one can see the close analogy which holds between animal and plant bacteriology by noting the various channels which the author mentions through which bacteria infect plants, wounds for instance, natural openings, and stomata. Similar analogies can be observed by the facts which are brought out concerning the period of incubation which holds for plant diseases as well as for animal infections and in the treatment of the topic of germicides. These analogies, however, persist only to a certain point. Thus the rapidity with which bacteria infect plants depends upon conditions much more under the observation of the pathologist than in the case of animals. A juicy water-logged plant becomes infected far more quickly with a given organism than a dry, spongy specimen. In no instance can one explain so simply the variations seen in human and animal infections and we only confess our ignorance when we speak of heightened or lowered resistance. In other respects also the effect of bacterial growth upon plants is more easily explained by physical or chemical laws than with animals, as in those infections in which the invading organism secretes substances exerting a solvent action upon the cell wall, substances acting as enzymes and like enzymes destroyed by boiling and the action of chemicals. Indeed there are many phases in the reactions which occur between microorganisms and plant tissues which suggest interesting fields of speculation to the student of human disease. In certain respects the reaction which plants show towards bacteria differs essentially from the reactions seen in man and the animals, there being, namely, no production of antibodies in plants, the work already done along this line failing to reveal these bodies.

The subject of symbiosis is treated by Dr. Smith at considerable length and illustrated by an exhaustive description of the root nodules of the Leguminosæ about which we have heard so often of recent years. In this condition an organism known commonly as *Bacillus radicicola* or *Pseudomonas radicicola* develops in the roots of plants like peas or beans and conveys nitrogen to them. Is this a true example of symbiosis, that condition in which two plants develop together, not antagonistic one to the other as in the case of parasites, but mutually helpful? This difficult question is discussed with great minuteness by Dr. Smith who concludes that the evidence thus far presented in regard to this much mooted case of true bacterial symbiosis is by no means conclusive and that much of the experimental work requires repetition and confirmation.

Such references as these indicate in general the scope of the first part of Volume II. The latter part of the volume is devoted to certain bacterial diseases of plants involving the vascular system, including a disease of cucumbers known as Cucumber Wilt, one of the cabbage termed Dry Rot or Brown Rot, and Wakker's bacterial disease of hyacinths or Yellow Slime. In each case the disease is carefully portrayed, the associated bacteria clearly and amply described and the experimental evidence given which has established the etiological relationship of the organism to the infection.

The two volumes are published by the Carnegie Institution of Washington, as a result of which more profuse and abundant illustrations are shown than in the ordinary text-book. The great value of the work, its thorough scientific character, the wealth of its bibliography all combine to make it a valuable addition to the library of the medical bacteriologist despite the fact that in its plan and scope it is designed especially for the plant pathologist.

W. W. FORD.

Genito-urinary Diseases and Syphilis. By HENRY H. MORTON, M. D. Illustrated. Third edition, revised and enlarged. $5. (*Philadelphia: F. A. Davis Company, 1912.*)

The second edition of this book appeared in 1906, and since that date the spirochæta pallida has been discovered. In addition much new work has come out on the prostate and tumors of the bladder, and most valuable new methods of treatment by the use of phenolsulphonephthalein, and salvarsan also have been put in practice. The results of all this work are incorporated in Dr. Morton's treatise, so that in its present form the book is modern, and may serve as an introduction to more comprehensive works on the same subject. Some of the illustrations are good, but many are so poor as rather to detract from than add to the value of the book.

E. Merck's Annual Report of Recent Advances in Pharmaceutical Chemistry and Therapeutics. Vol. XXV. 1911. (*Darnstadt: E. Merck Chemical Works, 1912.*)

These reports are valuable to the scientific pharmacologist and therapeutist, as they contain much information on newer drugs which it would be difficult to obtain otherwise without long search in many journals. In this number there are special chapters on the glycerophosphates, and digitalis glucosides and allied drugs. Those desirous of securing this report, can obtain copies for fifteen cents from Merck & Co., New York.

Diseases of the Liver, Gall Bladder and Bile Ducts. By HUMPHREY DAVY ROLLESTON, M. A., M. D. (Cantab.), F. R. C. P. Second edition. $9 net. (*London: Macmillan & Co., Ltd., 1912.*)

Some years ago the writer had the pleasure of reviewing the first edition of this work. The favorable view which was then expressed has been fully supported by the best test of the value of a book—the extent to which it is used. This work has always proved a perfect storehouse of knowledge and has been of great assistance. A second edition is very welcome, especially as any work done by Dr. Rolleston is particularly satisfactory for the American reader, because he is so familiar with American literature and work. It has sometimes seemed as if he knew more about what was going on here than we did ourselves.

The general arrangement of the book is much as in the first edition. The first and largest part of the work is devoted to the diseases of the liver, after which those of the gall bladder and bile ducts are considered. Anatomical peculiarities and hepatoptosis receive very full consideration and are followed by the discussion of the diseases of the blood vessels including thrombosis and pylephlebitis. The author has not changed his views as to the relative unimportance of functional disturbances of the liver, and it is probable that the public would be rather surprised if they could see the small space given to this subject in a systematic treatise. The subject of "biliousness" occupies a very small space and in this connection the author points out that symptoms so designated and often assigned to the liver are, as a rule, not due to primary failure on its part, but to disturbance elsewhere, particularly in the alimentary tract.

There is a clear description of the pericarditic pseudo-cirrhosis of the liver, a subject about which there is considerable confusion. The account given here seems extremely clear. Probably one turns to the subject of cirrhosis with the greatest interest, for there is no disorder so obscure in some aspects and so difficult to discuss in a clear and comprehensive way. As was said in the previous review, this is a very practical and satisfactory discussion of the subject. The description of the pathological changes is particularly good. There are many points in reference to cirrhosis about which we are in doubt. Take for instance the occurrence of ascites which in some cases appears to be a terminal event, in others due to a chronic peritonitis, sometimes local. The various possibilities are fully discussed. The important subject of syphilis of the liver receives adequate discussion.

Rarer conditions, such as actinomycosis, hydatid cysts, cystic disease, and primary malignant disease are thoroughly taken up. Secondary malignant disease receives a full discussion. To the

subject of jaundice a section is given, for although a symptom and not a disease, yet a special consideration of it is proper. The classification here given is into *extra-hepatic* or *obstructive* and *intra-hepatic, toxæmic* or *hæmo-hepatogenous*. These are subdivided in a most methodical way, there being no less than fourteen headings under the discussion of jaundice due to pressure on the bile-ducts from without. There are special sections on jaundice on the new-born, icterus gravis, infectious jaundice, and acute yellow atrophy. It is perhaps surprising to find how little space comparatively is required for the consideration of cholecystitis apart from cholelithiasis. This latter subject requires much more space and is thoroughly taken up. This section is an excellent example of what the discussion of such a subject ought to be. It is sufficiently full and at the same time not prolix. The summing up of the conditions which demand operation is excellent and a satisfactory statement of opinion on this subject, about which there is so much room for difference of opinion.

Altogether this work may be regarded as a model of what a treatise dealing with the diseases of a single organ should be. There is a proper balancing of various sections and a clear arrangement of heads and sub-headings which aids understanding so much. It is the best work on the subject which we have and is to be highly recommended. We desire to congratulate the author on the second edition.

Health and Medical Inspection of School Children. By WALTER S. CORNELL, M. D. Illustrated. (*Philadelphia: F. A. Davis Company, 1912.*)

Dr. Cornell has written a large work, which he divides into three main sections: 1, Medical Inspection; 2, Hygiene; 3, Defects and Diseases. As director of medical inspection of public schools in Philadelphia he writes from large experience, and his work is valuable. It would be more so were it not so comprehensive; to the first section, or Medical Inspection, which seems to us should be the most important one, the author gives only 150 pages; to Hygiene less than 50; and over 400 (!) to the defects and diseases of school children, and yet he does not pretend to be writing a medical treatise on these diseases. Exactly for what class of practitioners this book is intended is not clear. Both nurses, who are now so much and so profitably used for school inspection work, and young medical inspectors of schools will find special parts of it useful. The importance of the subject is now, it may be said, generally recognized and where medical inspection of schools is to be put in force for the first time, this book will prove a helpful guide in the hands of those who have to organize the work. It is somewhat marred by redundancy, and many of the illustrations are wretched—they are so small or so smudgy in reproduction as to be absolutely worthless. Innumerable photographs of children with adenoids are quite unnecessary, and those of skin lesions are not helpful. It is a pity such poor pictures should have been used. There are also certain statements made by Dr. Cornell in regard to contagious diseases, which need further support and evidence before they can be accepted as proven. The book is full of suggestions for those who have had little or no experience in this line of work, which covers a very broad field, and requires well trained physicians to fill the posts of school inspectors.

Obstetrics. A Text-Book for the Use of Students and Practitioners. By J. WHITRIDGE WILLIAMS. Third enlarged and revised edition. (*New York and London: D. Appleton & Co., 1912.*)

The popularity of this text-book, now published in a third edition, must be gratifying not alone to the author but to all who are interested in placing obstetrics upon a dignified, scientific basis—a position, it must be confessed, which has not been approached until the present generation. An increasing demand for this work indicates that fewer and fewer teachers and practitioners are content with knowing how to care for patients at the time of labor and immediately thereafter. It is dawning upon those given charge over the training of medical students that interwoven with obstetrics are a number of sciences including not only embryology, histology, physiology, and pathology but also zöology, chemistry, and physics. The readers of this volume become familiar with the relation of these fundamental subjects to the science, and consequently to the rational practice of obstetrics.

In accord with his scientific attitude the author never hesitates to point out the gaps in obstetrical knowledge, but rather accepts these as an opportunity to encourage investigation. The student will also find in the numerous contributions of the author himself an incentive to undertake original work. Indeed it is the first-hand knowledge included in several of the chapters that makes them particularly attractive; especially is this true of the sections on the pelvis, the toxemias of pregnancy, and puerperal infection.

The emphasis given the study of the pelvic outlet is justified because contraction of the outlet is somewhat more common than of the inlet, and also because serious dystocia may occur in cases of funnel pelvis. Generally, in these cases pubiotomy is the treatment of choice; this operation, when feasible, affords facility in the delivery and, furthermore, by permanently enlarging the pelvic cavity proves a curative measure. The treatment of labor with other types of contracted pelves is clearly and logically discussed, greatly simplifying the problem of the management of such cases.

In contrast with the definite information regarding the pelvis, now placed at the disposal of the obstetrician, very little is known of the nature of autointoxication during pregnancy. The author maintains that finding different lesions in fatal cases we must believe there are several kinds of toxemia of pregnancy, and insists that knowledge of these conditions will advance more rapidly if the pathological classification is adopted.

The author holds an uncompromising view of the responsibility of the doctor and the nurse in the aseptic management of labor. In fairness he cites the work of those investigators who have found pathogenic bacteria in the vagina during pregnancy; but to his mind it is not proven that these organisms may cause infection in the individual from whom they were obtained. The straight-forward statements which attribute the occurrence of infection to lax surgical technique in the conduct of labor will inspire resentment in anyone who is negligent of such details. But this teaching is certainly most wholesome, for it puts the obstetrician on guard; it is supported, moreover, by the best clinical and experimental evidence.

The entire book has been revised; not a single chapter has failed to undergo the alterations that were needed to bring it up to date. Thus, in the section on the development of the ovum we find incorporated what has been learned from the lately published descriptions of several early specimens. Yet, unfortunately, we still possess but meagre information regarding the formation of the fœtal membranes in man; and, so long as it continues to be necessary to fall back upon the lower animals for a description of the development of the amnion and the chorion, this chapter will be a bewildering one for the medical student.

Practitioners wishing to keep abreast of the times will find this new edition very useful. Innovations in operative obstetrics, as pubiotomy and extra-peritoneal Cæsarean Section, are critically discussed. The chapter on forceps is the most satisfactory that we have seen. The author's wide knowledge of the literature, his fairness in weighing evidence, and his clear, concise way of writing are qualities which have helped to give this volume a distinguished place among the text-books on obstetrics

A Treatise on Diseases of the Hair. By GEORGE THOMAS JACKSON, M. D., and CHARLES WOOD MCMURTRY, M. D. (*Lea & Febiger, Publishers, 1912.*)

The contents of this work have been gathered from text books on diseases of the skin, and from original articles on this subject. The reference bibliography given in footnotes, enhance the value of the volume.

While the text on the anatomy of the hair and hair follicle is a summary of dry facts, it is arranged in an interesting manner. Many illustrations, among which are six colored plates from Darier's work, give an adequate representation of the histological features of these structures.

The chapters on physiology and hygiene are written in a popular and entertaining way. Much good advice is given in regard to the ordinary care of the scalp, and this can be read with pleasure and profit by anyone.

The various diseases that are described, have been divided into four groups. Under "Essential Diseases of the Hair," are considered those peculiar to the hair alone. The second group comprise the "Inflammatory Diseases of the Hair Follicle." Next come the "Parasitic Diseases of the Hair." The "Diseases of the Hair Secondary to Diseases of the Skin" form the last group, and under this heading are described those diseases of the skin which may attack the scalp.

Unquestionably the most interesting chapters are those on ring worm and seborrhœa. Sabouraud's work on these diseases has been fully abstracted. Many half-tone illustrations of the various forms of ringworm, with the cultural characteristics of the infecting fungus, are shown. His method of treating this obstinate disease with the Xrays, and of measuring the dose is also clearly demonstrated. Seborrhœa capitis, too, is well described and illustrated. The formula for the culture medium, by which Sabourand gets the best result in cultivating his microbacillus, is given, and also the directions for getting a pure culture of this bacterium.

The book should be welcomed heartily, as it is a valuable addition to our library on dermatological subjects.

Hypnosis & Suggestion. By W. HILGER, M. D. (Magdeburg.) Translated by R. H. FELKIN, M. D. $2.50. (*New York: Rebman Company, 1912.*)

This handbook of 224 pages opens with an introduction by Dr. Van Renterghem, of Amsterdam, who gives a brief but comprehensive survey of the rise and progress of psychotherapy during the last sixty years. A well-deserved tribute is paid to the memory of Liébeault, who, following up the work of Braid, introduced hypnotic treatment, as it is now used, into medical practice. The book is divided into four parts and deals with (1) nature and methods of hypnosis and suggestion; (2) suggestion and will; (3) influence of the will's action, suggestion, and various psychological factors in the disturbance of the area of sensation; (4) disturbances of the reflex activity and their treatment.

The book is written in a simple and clear way, but is rather superficial and unconvincing. Cases of alcoholism, morphinism, acute articular rheumatism, asthma, heart affections, retention of urine, constipation, etc., are reported which the author claims have been cured either by hypnosis, or by suggestion in the waking state.

Most of the cases reported, however, have been imperfectly analyzed, and there is very little account of the duration of the cures.

The author should be congratulated on being more honest than the majority of his confrères as he admits that, in the treatment of his cases by hypnosis or suggestion, he may employ hydrotherapy, dietetic measures, and drugs as occasion may demand.

Selected Papers on Hysteria and Other Psychoneuroses. By PROFESSOR SIGMUND FREUD. Translated by A. A. BRILL, *Journal of Nervous and Mental Disease*, Monograph Series No. 4. Second edition. (*New York: 1912.*)

It is exceedingly gratifying to think that sufficient interest has now been aroused in Freud's works to warrant a second English edition of Brill's able translation. The chapters are taken from three different volumes of Freud's works, and have been so selected that one can get an excellent idea of his views in regard to hysteria and the other psychoneuroses. The technique of the treatment of these cases by means of psycho-analysis is fully dealt with, and numerous cases are reported, some of which are gone into in detail so that one sees just how the technique is utilized. There is absolutely no doubt but that Freud has been able to shed much new light on the psychoneuroses, and by means of psychoanalysis one can get to a point where some of the curious manifestations of these states can be understood and frequently explained. He believes that hysterical symptoms are the symbolic expression of the realisation of a repressed wish, and serve as a source of gratification to the patient. These symptoms can be made to disappear, and will not return if one is successful in thoroughly awakening the memories of the causal process with the accompanying affect, and if the patient can be got to thoroughly discuss the process and give free play to the affect. When these views were first promulgated a great many physicians jumped to the conclusion that by means of psychoanalysis the whole constitution of the individual could be changed, but Freud has stated specifically that one must rest content if he can remove the disease for which such a constitution shows a tendency, and that he must not hope or expect to be able to change the constitution of the individual.

One of the most frequent objections which one hears in regard to psycho-analysis is that in certain cases there is a great danger of suggesting things which may be harmful to the patient. To that objection Freud replies by saying that it is not possible to press upon the patient things which he apparently does not know, or to influence the results of the analysis by exciting expectations.

Great emphasis is laid upon the analysis of dreams—both "day dreams" and night dreams—as they give the most direct access to the unconscious. No case can be adequately treated without an investigation of the dream states.

With most of Freud's general principles one must be in entire agreement and certainly a tremendous impetus has been given to the study of the psychoneuroses by his views, but one hesitates to accept all his ideas and theories in regard to the rôle of infantile sexuality especially as most of his deductions are drawn from the "fancies" and "reminiscences" of psychoneurotic individuals.

Another matter that may be criticised is the fact that he tends to draw very sharp distinctions between various psycho-neurotic states, for instance between neurasthenia and the anxiety neuroses. Neurasthenia is characterized "as a monotonous morbid picture in which as shown by analysis psychic mechanisms play no part," whereas the anxiety neuroses are said to have a very strongly marked sexual etiology. His proofs of anxiety neuroses being a separate disease entity are not especially convincing, and his last argument is distinctly weak, *e. g.* "if the separation of anxiety neurosis from hysteria be denied one will also be unable to maintain the so painstakingly acquired distinction between neurasthenia and hysteria, so indispensable for the theory of the neuroses."

Two further chapters are added in this second edition to those contained in the first, one on "Wild" Psycho-analysis in which it is proved to be exceedingly important to thoroughly learn the technique of psycho-analysis; and the other on "The Future Chances of Psycho-Analytic Therapy."

Building a Profitable Practice: Being a Text-Book on Medical Economics. By THOMAS F. REILLY, M. S., M. D., etc. (*Philadelphia and London: J. B. Lippincott Company, 1912.*)

Dr. Reilly's book will doubtless be popular and have a large sale, for it contains instruction on many points about which the young practitioner, when leaving the medical school, is usually in ignorance. But we cannot commend it. Its tone is lacking in dignity on many important questions of ethics, and the standards of the medical profession would not be raised were this work its only guide. The rules of practice, as laid down by the author, will help the beginner to make his way financially, but they are not such as to give him high ideals or make him feel that in the practice of medicine there is a higher and finer end to be attained than a well-filled pocket book.

Infant Feeding. By CLIFFORD G. GRULEE, M. D., Assistant Professor of Pediatrics at Rush Medical College. Illustrated. $3. (*Philadelphia and London: W. B. Saunders Co., 1912.*)

The book, "Infant Feeding," of 295 pages, is based on a course of lectures given to the students of the Rush Medical College. In it the author aims to combine the knowledge of the scientific processes which underlie infant feeding in such a way that they may be applied in an efficient manner by the practising physician.

The volume comprises four main divisions: Part I relates to the "Fundamental Principles of Infants' Nutrition"; Part II, to the "Nourishment of the Infant on the Breast"; Part III, to "Artificial Feeding"; and in Part IV "Nutrition in other conditions" is considered.

Much of the work is a compilation of facts which may be found in other text-books on this subject, and, for that reason, a summary in detail is not necessary. The importance of breast feeding is properly emphasized. The injunctions given apropos of the promiscuous and unthinking use of proprietary foods are admirable, and the advocacy of longer intervals between feedings is in the trend of modern thought.

While the views in general accord with the opinions held by those most actively engaged in teaching pediatrics, exception may properly be taken to certain views therein expressed. For example, in Part III, Chapter 12, "Nutritional Disturbances of the Artificially Fed Infant," the attempt clearly to classify these disorders is made. The grouping which is advocated is based partly on the classification suggested by Czerny and partly on that laid down by Finkelstein. The shortcomings of such a classification are best emphasized by the grouping of ileo-colitis, cholera infantum, dysentery, etc., under "Intoxication," conditions which are clinically dissimilar, even widely differentiated, with known pathological and etiological differences. Such a classification is complicated and inaccurate, and is to be condemned from both a scientific and practical standpoint. The disregard also of the streptococcus in milk as a direct infecting agent (page 113) is unwise, a fact indicated by the recent epidemics of "Septic Sore Throat."

The Bibliography is an asset of value to the book, and the index is complete. The author appreciates the value of illustrations; some of these are excellent, while others, especially those of the stools, are very poor.

Anæsthetics and Their Administration. By SIR FREDERIC W. HEWITT, M. V. O., etc. Fourth edition. Illustrated. $5. (*London: Macmillan & Co., Ltd., 1912.*)

There are few problems that come to the anesthetist that are not discussed in this revised edition. The discussion of the theoretical and experimental physiology of anesthesia are especially interesting and instructive, and the author also offers suggestions for further investigations. He is very conservative in the conclusions he draws from the experimental work. The individual variation of patients has so much to do with the administration of an anesthetic that it is very difficult to give rules or to describe any method of procedure that will apply to all for the administration of an anesthetic. This phase of the subject has been handled very skillfully.. Some of the newer methods of administration which are not yet thoroughly established are merely touched upon, *e. g.*, intratracheal insufflation is dismissed with one paragraph. Two new chapters have been added in this edition, one on local and regional anesthesia, the other on medico-legal aspects of surgical anesthesia. The book is well written and illustrated. It is complete, without being too cumbersome, making it useful both for the student practitioner and special anesthetist.

A Laboratory Hand-Book for Dietetics. By MARY SWARTZ ROSE, Ph. D. $1.10. (*New York: The Macmillan Company, 1912.*)

This is an excellent work, one that should prove most useful to nurses as well as doctors. Dr. Rose has compiled many tables showing the nutritive value of a great variety of foods. With these tables it is easy for anyone to calculate a food value and requirement for any person at almost any age and to prepare a suitable dietary under a doctor's order. The tables are prepared not only with the weight in pounds and ounces but also in grams, but the average price of the articles is given, so that the cost of the dietary is readily computed. The caloric value of the foods is also tabulated. In addition to the tables Dr. Rose has also prepared problems to be worked out, so that this handbook is most instructive, and to be warmly commended as a clear exposition of a difficult problem.

Progressive Medicine. Edited by HOBART AMORY HARE, M. D., assisted by LEIGHTON F. APPLEMAN, M. D. Vol. IV. (*Philadelphia and New York: Lea & Febiger, December, 1912.*)

Except for two chapters—Practical Therapeutic Referendum and Surgery of the Extremities, Shock, Anæsthesia, Infections, Fractures, Dislocations and Tumors—the entire volume is given over to the discussion of surgical problems dealing in large part with the abdominal and pelvic organs. The contributors are Bloodgood, Bonney, Bradford, Goodman and Landis, who furnish excellent résumés of the progress in the treatment of these various affections. This volume is valuable in giving the reader the views of leading operators all over the world on various difficult surgical problems.

Elementary Bacteriology and Protozoölogy. By HERBERT FOX, M. D., Director of the William Pepper Laboratory in the University of Pennsylvania. (*Philadelphia and New York: Lea & Febiger, 1912.*)

This little book is written primarily for the beginner in bacteriology and for the nurse, to give, as the author states, an "idea as to the world's economy especially in disease." The subject matter is carefully selected, the text is well prepared and the important pathogenic organisms described with accuracy although briefly. The book will doubtless serve a useful purpose in instruction in elementary bacteriology.

Principles of Microbiology. A Treatise on Bacteria, Fungi and Protozoa Pathogenic for Domesticated Animals. By VERANUS ALVA MOORE, Professor of Comparative Pathology, Bacteriology and Meat Inspection, New York State Veterinary College at Cornell University and Director of the College. $3.50. (*Ithaca, N. Y.: Carpenter & Co., 1912.*)

Seldom if ever has a text-book on bacteriology appeared in the English language which offers so much to praise and so little to criticise as this publication from the pen of Professor Moore.

Dedicated by him to those students who have worked under him in his own laboratory, it may well have been dedicated to all students of bacteriology regardless of whether they are interested in the medical or the veterinary sciences. Indeed the essential principles of bacteriology, its methods and technique are the same in all its branches while in addition the historical development of the science and its gradual evolution from chaos to clearness is indissolubly bound up with the investigations into the life history of microorganisms which cause diseases in animals. It is natural, of course, that in a book designed particularly for veterinary students certain diseases will be emphasized which seldom are touched upon in text-books upon the bacteria pathogenic for man. In many cases, however, these organisms are the ones most carefully studied in courses of bacteriology in medical schools and form a chief part of the armament of the teacher of this subject. More than a third of the book is given up to a consideration of the general principles of bacteriology and such topics as the isolation and cultivation of bacteria, methods of examination of cultures, microscopic study of specimens and the vital activities of bacteria are treated at length. Methods and technique indeed are emphasized throughout, but possibly the features which are of the greatest value in this book of Professor Moore's and in which it is superior to other text-books is the care and thoroughness which are devoted to descriptions of the various microorganisms such as the *Streptococcus pyogenes*, the *Micrococcus aureus*, the *Bacterium anthracis*, the *Bacterium mallei*, the *Bacillus lactis aerogenes* and the tubercle bacillus. Particularly to be praised is the author's treatment of the organisms causing hemorrhagic septicæmia in animals, a chapter in bacteriology in which the majority of our text-books are either hopelessly muddled or entirely inadequate. The actual number of organisms described is somewhat small and this may excuse the author for not mentioning the *Bacillus aerogenes capsulatus* of Welch and Nuttall, the most widely distributed anærobic organism in nature. The chapter on protozoa is rather short, but considering the fact that the book has less than 500 pages the space devoted to this subject represents probably as much as the author felt could be allowed. The classification adopted for the protozoa is practically that of Calkins, the classification for the bacteria being that of Migula. The discussion of filtrable viruses also seems scanty when we think of the importance of the subject and remember the classic investigations of American bacteriologists upon that widely distributed disease, hog cholera. The treatment of specific bacterial products is exceptionally good, excellent descriptions being given of the precipitins, and agglutinins, and the opsonins. The final chapter of the book on Immunity and Vaccine Therapy is very brief, but this may be an advantage in view of the long and complicated discussions of the subject in other text-books.

This book of Professor Moore's is most highly to be recommended to all students of bacteriology, and especially to new workers in this field who desire to acquaint themselves with the fundamental elements of the subject.

The Chemic Problem in Nutrition (Magnesium Infiltration). By JOHN AULDE, M. D., etc. Illustrated. (*Philadelphia: John Aulde, M. D., 1912.*)

The author has strayed into many fields of science more or less unfamiliar to the practicing physician and apparently unfamiliar, at least in part, to himself. Many of his historical statements and verbatim quotations are correct. However, his use of periods instead of interrogation marks at the end of innumerable sentences is much to be regretted. Illogical deductions instead of scientific proof as well as incomprehensible statements characterize the book throughout. There is no excuse for the body of the publication. L. G. R.

Die Experimentelle Pharmacologie als Grundlage der Arzneibehandlung. Von DR. HANS H. MEYER und DR. R. GOTTLIEB. (*Berlin-Wien: Urban u. Schwarzenberg, 1911; New York: Rebman Company.*)

The second edition of this most admirable text-book deserves a good deal of attention. In the first place, the subject is presented in a very original way, in as much as the drugs are classified according to the anatomical structures upon which they act. In the chapter of the pharmacology of the heart, drugs are described, which exhibit cardiac action. This scheme of presentation has a great many advantages over the one commonly found in text-books of pharmacology. A physician dealing with a specific pathologic condition will find it easy to familiarize himself with the details of the action of the various drugs which might come into consideration. The student will find much inspiration in this book, and it may well be said that to the pharmacologist it gives a great deal of pleasure. This text-book undoubtedly presents the best known scientific basis for the therapeutic use of drugs. It is to be hoped that an English edition will appear in the near future.

Nachweis und Bestimmung von Giften Auf Biologischem Wege. Von DR. H. FÜHNER. $2.25. (*Berlin-Wien, Urban & Schwarzenberg, 1911; New York: Rebman Company.*)

This practical guide for the detection and estimation of organic and inorganic poisons deals with the biological methods which are used in pharmacologic and toxicologic work. In a clear and elementary way, methods are described in detail for the determination of the antiseptic action of drugs, the standardization of digitalis, epinephrine, local and general anæsthetics, antipyretics, thyroid and the detection of muscarine, strychnine, veratrine, curarine, nicotine, salicylic acid, etc. Various cells of vegetable and animal origin serve as test objects. Numerous illustrations are inserted into the text and help to make the methods very comprehensive. This book is primarily intended for use by toxicological chemists and physicians who have to deal with medico-legal cases. The author remarks in the preface that the known methods are relatively few in number, and that some of them are not yet worked out thoroughly. In spite of these deficiencies we believe that the author can be congratulated on his efforts.

Manual of Medicine. By A. S. WOODWARK, M. D. $3.75. (*Edinburgh, Glasgow and London: Henry Frowde and Hodder & Stoughton, 1912.*)

Dr. Woodwark says in his preface that he hopes to fulfill a two-fold purpose with this book: that of supplying a *vade mecum* for the student clerking in the wards or out-patient department, and a convenient reference for the busy practitioner. We hope, in spite of our dislike for such manuals, that the author's desire may be fulfilled to his own satisfaction. It is a manual which would be of service to nurses also. The author has condensed the larger text-books of medicine satisfactorily, bringing out the main points of each disease, but medicine cannot be served up in this way any more than its sister, surgery, and be really helpful to a young practitioner who wants to advance. He had better search the larger text-books than refer to the primers of the subject he is studying.

Stuttering and Lisping. By C. W. SCRIPTURE, Ph. D., and M. D. $1.50. (*New York: The Macmillan Company, 1912.*)

It is only within a few years that doctors have studied stuttering and lisping scientifically, and this book is the product of such study. It is unfortunately true that few physicians have the necessary patience and time to give to patients suffering from these troubles, and the poor stutterer, as a result, often enough

has a miserable time in life. Dr. Scripture's book will fill a long felt want, for it is but a small manual which any interested physician can easily master in a short time, and an intelligent patient can also gain much from a careful perusal of it. The author, who has been for some years a special student of these conditions, describes stuttering as a psychoneurosis, and the best methods of treatment, and divides lisping into three forms—negligent, organic, and neurotic—and gives a long list of exercises to overcome this disturbance of speech. The book has been carefully and well prepared, and may be warmly commended.

Fiske Fund Prize Dissertation No. LV. Medical Inspection of Schools. By ALLEN G. RICE, M. D. (*Providence: Snow & Farnham Company, Printers, 1912.*)

This dissertation is an interesting review of the development and growth of medical school inspection in this country. The author has gathered much information as to how the schools are inspected, and how parents and boards of health are notified when children are ill, and his essay is of value to a large body of physicians who take an interest in this branch of civic welfare.

Year Book of the Pilcher Hospital. No. 2. (*Philadelphia: J. B. Lippincott Company, Philadelphia, 1912.*)

The second year book of the Pilcher Hospital is an interesting production. Some of the papers are quite brief, so that the volume is not large, but well worthy of note as an expression of the excellent work done in this hospital. Many of the papers are illustrated. The articles are classified under the following headings: Fractures, cancers, benign growths, affections of the digestive organs, urological cases, not classified, and appendices with twelve subjects reported on. The wealth of material of the staff, which is composed of only three operators is great; and such a volume as this shows how much could be done by others if they would only take the same trouble as the Pilchers to publish their records—for records of private cases often are of as much value as those from public hospitals. The Doctors Pilcher are to be heartily congratulated on their Year-Book from every point of view.

A Practical Medical Dictionary. By THOMAS LATHROP STEDMAN, M. D., etc. Second Revised Edition. Illustrated. $5.00. (*New York: William Woodard Company, 1912.*)

The second edition of this excellent dictionary appears within about a year of its first publication, showing the well-merited appreciation it has received from the medical profession. In its present form it contains 2000 more words than in the original, but its general appearance remains the same; and it is a pleasure to have the opportunity to recommend it anew.

X-Ray Diagnosis and Treatment. Review of DRS. BYTHELL and BARCLAY'S book.

The simplicity and concise manner in which this book is written should make it especially valuable to the student and general practitioner.

It is very gratifying to find a book which is so largely devoted to the fundamental principles of interpretation of X-Ray shadows.

Probably the weakest part of the book is that devoted to head and sinus work. Stereoscopic radiography of all head cases taken at one or two good constant angles will obviate the extreme distortion produced by angulation for certain difficult parts.

The authors' interpretation of early phthisis seems a little exaggerated, remembering that various other infections as chronic influenza and low grade pneumococcus will give practically the same radiographic picture.

The chapters on œsophageal stenosis, and stomach and intestines are especially good.

More or less divergence of opinion is, of course, to be expected in such a rapidly developing field as radiography. Dr. Bythell and Dr. Barclay have given us their opinions and experiences, and to them we are greatly indebted.

On the whole one can regard this book as a most worthy addition to the literature on radiology. C. A. WATERS.

Life of Sir William Tennant Gairdner, K. C. B., M. D., LL. D., F. R. S., Regius Professor of Practice of Medicine in the University of Glasgow. By GEORGE ALEXANDER GIBSON, M. D., Sc. D., LL. D.; Senior Physician to the Royal Infirmary, Edinburgh. With a selection of papers on general and medical subjects. (*Glasgow: James Maclehose & Sons, Publishers to the University, 1912.*)

Rather more than one-third of this handsome volume of 817 pages is devoted to the life and career of Sir William Gairdner and the remainder is devoted to judicious selections from his papers on general and medical topics.

The story of his life is given very judiciously in a series of chapters arranged somewhat differently from usual biographies. We are told of his early life, his hospital and medical training, his life in Glasgow, his marriage and family, his university and hospital labors, his medical and scientific work, his political, theological, and religious views, and his personal character.

His life is presented to us not so much chronologically as topically, and the reader is able to view it as a whole and to estimate his achievements. He unquestionably possessed a mind of no ordinary scope, both as a clinician and as an original investigator. He had broad views of the relation of medicine to science. He worthily expressed this in his declaration that "*the true art of medicine is that it is doubly founded, first on experience and then on reasoned experience.*" He constantly reiterates that to know medicine one must have "the knowledge of *things* as opposed to *words* and *abstract ideas.*" He did not ask for a hasty diagnosis but for a thorough one. These principles are especially applied in his papers on purely medical subjects, several of which are printed in the volume. They are models of clear thinking and accurate presentation and deserve careful reading now, although some of them were written a half century ago.

He was a skillful clinician, a painstaking teacher, an efficient public health officer, and a ready writer. He had the devoted affection of pupils and colleagues, and the confidence of the public.

An interesting account is given in the volume of his visit to America in 1891, and some letters are printed containing personal references to Pepper, Holmes, Weir Mitchell, Osler, the Bowditches, and others whose names are familiar. He was not critical, but appreciative, and showed everywhere the same child-like spirit and keen interest in what he saw which characterized his home life.

The book contains many pleasant anecdotes, some of which, especially those as to his absent-mindedness are not unfamiliar. It is most interesting and deserves to be read by physicians.

The Anatomy of the Human Eye. Illustrated by Enlarged Stereoscopic Photographs. By ARTHUR THOMPSON, M. A., M. B., F. R. C. S. (*Oxford: At the Clarendon Press, 1912.*)

The study of the anatomy of the eye by means of stereoscopic pictures is a welcome change from the study of the anatomy by means of the usual text, and the accompanying diagrams and pictures, which have, in many instances, been reproduced for years in the newer and older text-books. This is an entirely new set of pictures to the number of sixty-seven, with a carefully written description of each one, and the work marks a distinct step forward in the make up of ophthalmological text-books and

atlases. This series of plates enables one to see anatomical details at a glance, without effort on the part of the imagination to supply the perspective. The pictures are carefully accurate, and are not overdrawn for the sake of effect. Most students must view such pictures with real interest, and a vivid impression will be left on their minds which pages of reading matter might hardly as effectively accomplish.

The painstaking care and work on the author's part deserves the grateful appreciation of all readers of ophthalmologic literature, and a work such as this should be a lasting monument to the wisdom of the accomplished author. We heartily commend this work to anyone taking up the study of eye diseases, and assure him that he will be repaid manifold for the slight trouble which the use of the stereoscope will necessarily require.

We hope that this work will be handily available in all clinics where medical students are instructed in ophthalmology; for by means of it many rough paths on the part of instructor and student will be smoothed over, and the efforts of each very much lessened.

B. B. BROWNE, JR.

Scientific Memoirs. By OFFICERS OF THE MEDICAL AND SANITARY DEPARTMENTS OF THE GOVERNMENT OF INDIA. (*Calcutta: Superindent Government Printing, India, 1912.*)

New Series No. 51. A Streptothrix Isolated from the Spleen of a Leper. By MAJOR W. G. LISTON, M. D. and CAPTAIN T. S. B. WILLIAMS, I. M. S. 1/4.

No. 52. Dysentery in Hazaribagh Central Jail—January, 1910-March, 1911. Being the Report of an Inquiry Carried out by CAPTAIN R. T. WELLS, M. B. 2/9.

No. 53. The Development of the Parasite of Indian Kala Azar. By CAPTAIN W. S. PATTON, M. B. 1/2.

The first of these three reports is a very brief study by Major Liston and Captain Williams of a new (?) streptothrix. The growth of the organism on lemco-agar is well described, and there are some beautiful colored micro-photographs which demonstrate its morphology finely.

Captain Wells has added another interesting chapter to the study of dysentery, which is so frequently obscure in its causative, and laboratory workers will find this memoir well worth careful consideration.

The third paper, by Captain Patton, also illustrated by a fine photogravure plate showing the development of the parasite of kala azar, is another one of those important contributions coming from the medical officers of the English army stationed in India. Few of these scientific contributions will have many readers, but special workers must have these publications close at hand, since they throw light on many questions which are still unsolved.

Oxford Medical Publications: Pathology of the Eye. By P. H. ADAMS, M. B., etc. $1.50. (*London: Henry Frowde, and Hodder & Stoughton, 1912.*)

This little book may doubtless be found of value to those who may wish to rapidly look up pathological points about the eye; for it is a convenient little handbook. It is probably a little too concise, and in many places the reading matter suggests a too brief discussion, when often cold facts are stated and then left to stand without further amplification. For the scientific reader this volume will have but little value.

Had the author, wishing to keep his volume small, devoted more specific attention to the consideration of lesions which are peculiar to eye tissues, and allowed less space to the study of inflammations which follow the same course in the eye as they do in other tissues, he would have produced a volume of more interest. The study of the eye changes met with in Glaucoma, and the consideration of the ætiological pathological factors involved in cataract and sympathetic ophthalmitis are insufficient for any comprehensive understanding of the subject. The book limits itself to the pathology of clinical cases, no attention being given to experimental pathology. In a word, the material of this work is readily available in some of our larger text-books on the eye, and it deserves specific approval only as a convenient little volume.

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Oxford Medical Publications: Kidney Diseases. By W. P. HENINGHAM, M. D., etc. With Chapters on Renal Diseases in Pregnancy. By HERBERT WILLIAMSON, M. D., etc. $5.50. (*London: Henry Frowde and Hodder & Stroughton, 1912.*)

This is one of the best of the Oxford Medical Publications, and is especially interesting as being largely the result of the author's work in his own wards and hospital. It is not, as many other text-books, mainly the output of others. Dr. Heningham acknowledges his indebtedness to the labors of other writers, but throughout this book we feel that we are getting the personal views and conclusions of the author, and this makes it well worth reading. It is an excellent book for students. Dr. Heningham deals with the obscure origin and development of chronic nephritis in a broad manner, and does not attempt to classify too finely the different types of chronic nephritis either from a clinical or pathological standpoint. Of other diseases of the kidneys he gives a capital clear picture, one drawn from large bed-side experience. The author possesses unusual gift of style which makes his presentation of the subject most attractive. We only wish the case histories were in a smaller type than the body of the book.

A Manual of Auscultation and Percussion. By AUSTIN FLINT, M. D., etc. Sixth Edition, Revised and Enlarged. By HAVEN EMERSON, M. D. $2.00. (*Philadelphia and New York: Lea & Febiger, 1912.*)

One of the best of manuals, it is well that it should be constantly presented afresh to students. The late Austin Flint was one of America's few great physicians and his work on the lungs and heart marked an epoch in American medicine. His contributions are not as well known as they should be by the rising generation of young physicians, most of whom know his name only in connection with the murmur of aortic insufficiency, but his studies of the lungs are more important. Every student should study this manual with care, for Flint's method of presentation is exceptionally good, and once having obtained a mastery of the underlying principles as enumerated by him, the student will not find the diagnosis of conditions within the thorax so difficult as he is apt to do. There are only the classics which are ever fresh, and this manual may be justly regarded as one of them.

The Course of Operative Surgery. A Hand-book for Practitioners and Students. By PROF. DR. VICTOR SCHMIEDEN, Berlin. Second Enlarged Edition. Translated and Edited by ARTHUR TURNBULL, M. B. (Glasg.). $4.00. (*New York: William Wood and Company, 1912.*)

This is the first American edition of Schmieden's Surgery, but it corresponds exactly to the second and latest German imprint. It is one of the briefest manuals of surgery that has lately appeared, and should on this account be welcome to a large body of students. It is well and abundantly illustrated. Its brevity is due to the fact that the author describes only the main operations, so that the student is not overwhelmed by a mass of details. With a solid foundation in surgery based on a thorough knowledge of anatomy it is not difficult for a young surgeon to meet conditions as they present themselves, and he does not require all operations to be described in book form. Watching operators he can learn much that he could never acquire from

books, and if he has mastered the principles as set forth in this work he will have a firm base to build upon. This is, therefore, a more serviceable book for him than many larger treatises.

New Aspects of Diabetes. Pathology and Treatment. By Prof. Dr. Carl von Noorden, Vienna. $1.50. (*New York: E. B. Treat and Company, 1912.*)

A work by von Noorden on Diabetes must be of interest to all clinicians, since he is famous for his profound studies in this disease. The matter in this small volume was delivered in a course of lectures at the Post-Graduate Medical School of New York. The presentation of some of the underlying problems in this mystifying disease is excellent. He discusses the source of sugar, the rise in caloric production and its causes, the control of sugar formation and its disturbances, the theory and therapy of diabetes, and acetonuria with its influence on the treatment of diabetes mellitus. For physicians and students who are not acquainted with the latest work on this disease these lectures will aid largely to keep them informed on the modern trend of thought in regard to the chemical questions involved in this disturbance of metabolism.

Nutritional Physiology. By Percy Goldthwait Stiles. (*Philadelphia and London: W. B. Saunders Company, 1912.*)

The author is professor of physiology in Simmons College, and his small treatise is evidently intended for such classes of students as he has there; that is it is not intended for those who mean to study medicine seriously as a profession, but rather for those who desire and need a thorough grounding in the principles of the subject and for this class it is a good book, a clear presentation of the process of digestion. The author is to be congratulated on his success in dealing with a difficult topic in an interesting manner; and he has shown his skill in eliminating what was not essential to a satisfactory explanation of the topic.

Practical Physiological Chemistry. By Philip B. Hawk, M. S., Ph. D. Fourth Edition, Revised and Enlarged. $2.50. (*Philadelphia: P. Blackiston's Son & Co., 1912.*)

With a few additions necessitated by the latest work on enzymes, carbohydrates, proteins, blood, etc., that has appeared since the third edition of this work in 1910, the book maintains all its good characteristics which have made it popular with students. Dr. Hawk's work is well planned and written.

The People's Medical Guide. By John Grinshaw, M. D., etc. $3.00. (*New York: The Macmillan Company, 1912.*)

The sub-title for this work reads: Points for the Patient, Notes for the Nurse, Matter for the Medical Adviser, Succour for the Sufferer, Precepts for the Public." This makes one feel as though one had gone back half a century or more when such guides were common, but which little by little have disappeared, so that no longer in the home along side of a bible, a photographic album and a book of verse, on the center table in the parlor is a medical guide and counsellor to be found. On the whole the disappearance of such books can be looked on with approval, but there are parts of the world where unfortunates are bound to dwell and to whom such a book as this may be a god-send. Dr. Grinshaw in his volume of over 800 pages has put a mass of useful information on many matters in such a way as to be really serviceable for the class for whom it is intended. To compile such a work is no easy task and the author has done it with ability. He divides his subject into two sections on medicine, one on surgery, one on diseases of special organs, one on skin diseases, one on food and feeding and one on physical exercises, so that the medically uninformed reader may easily find what he wants. He writes in an easy, familiar, not too technical style, as a doctor should talk to his patients, and throughout he shows common sense. For intelligent people who are travelling in remote regions far from medical aid of any sort this volume would be a really valuable one for them to carry along. It is also a work which many a nurse would find often helpful.

Consumption in General Practice. By H. Hyslop Thomson, M. D., D. P. H. (*London: Henry Frowde and Hodder & Stoughton, 1912.*)

The book is a clear and brief presentation of the fundamental principles of the diagnosis, prognosis and treatment of pulmonary tuberculosis. It is intended for the general practitioner and is written in a direct, elementary style with no display of erudition. It is the expression of the experience of one man, not a coalition of the opinions of many men. What is thus lost in range and detail is gained in concreteness and force. The book will therefore be useful and stimulating to many without the leisure or inclination to study the subject thoroughly. There are some statements that will not receive general accord; for instance, that "at any time in the course of miliary tuberculosis the tubercle bacillus may be demonstrated in the circulation"; others that to the initiated are evidently errors, but errors that may occasion serious consequences if literally followed; for instance, that the initial dose of tuberculin for diagnosis is 0.1 cc. As is usual in treatises on tuberculosis the paragraphs dealing with the use of tuberculin in diagnosis are the poorest in the book. The directions for its use are insufficient, some of the directions are faulty and the interpretation of the results of the tests unsatisfactory.

L. H.

BOOKS RECEIVED.

Studies from the Rockefeller Institute for Medical Research. Reprints. Volume XV. 1912. 8vo. New York.

Progressive Medicine. A Quarterly Digest of Advances, Discoveries and Improvements in the Medical and Surgical Sciences. Edited by Hobart Amory Hare, M. D., assisted by Leighton F. Appleman, M. D. Volume III. September, 1912. 8vo. 253 pages. Lea and Febiger, Philadelphia and New York.

A Manual of Pharmacy. By M. F. DeLorme, M. D., Ph. G. Third edition, with 19 illustrations. 1912. 12 mo. 221 pages. P. Blakiston's Son and Co., Philadelphia.

Manual of Chemistry. A Guide to Lectures and Laboratory Work for Beginners in Chemistry. A Text-Book Specially Adapted for Students of Medicine, Pharmacy and Dentistry. By W. Simon, Ph. D., M. D., and Daniel Base, Ph. D. Tenth edition, thoroughly revised. With eighty-two illustrations, one colored spectra plate, and eight colored plates representing sixty-four chemical reactions. 1912. 8vo. 774 pages. Lea and Febiger, Philadelphia and New York.

NEW PUBLICATIONS.

The following three monographs:

Free Thrombi and Ball-Thrombi in the Heart. By J. H. Hewitt, M. D. Price, $1.00.

Benzol as a Leucotoxin. By Laurence Selling, M. D. Price, $1.00.

Primary Carcinoma of the Liver. By M. C. Winternitz, M. D. Price, 75 cents.

are now on sale by The Johns Hopkins Press, Baltimore. Other monographs will appear from time to time.

The Johns Hopkins Hospital Bulletins are issued monthly. They are printed by the LORD BALTIMORE PRESS, Baltimore. Subscriptions, $2.00 a year (foreign postage, 50 cents), may be addressed to the publishers, THE JOHNS HOPKINS PRESS, BALTIMORE; single copies will be sent by mail for twenty-five cents each. Single copies may also be procured from the BALTIMORE NEWS CO., Baltimore.